ENMC Impact Report 2022

Our year in highlights

EUROPEAN NEURO MUSCULAR CENTRE

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1 Message from Dr Alexandre Méjat, Chair of the Executive Committee

2022 was a year of particular intensity at the ENMC, for the best of our community.

After almost two years of limited face-to-face meetings, all participants of the ENMC workshops were eager to return to the friendly and open atmosphere of the meetings in Hoofddorp. This led to an exceptionally high number of 14 workshops organised during the year, which demanded that we organised up to three workshop weekends in a row in some months, particularly in the first half year of 2022. This required an equally exceptional mobilisation of the ENMC office and Executive Committee members, reinforced by Ms. Annelies Zittersteijn who generously provided her support during these unusual times. With special thanks to Ms. Esther Smit and Ms. Franziska Ott who coordinated all these workshops and ongoing operations at the ENMC. The experience acquired during the Covid-19 pandemic was used to continue to offer high quality hybrid format workshops.

The lessons of the pandemic also inspired the topic of the very first Themed workshop held from 1-3 April on the topic: "Remote delivery of clinical care and validation of remote clinical outcomes in neuromuscular disorders: a response to Covid-19 and proactive planning for the future."

These numerous workshops were an opportunity for young and talented researchers and clinicians, benefiting from the Early-Career Programme, to meet patient representatives and senior colleagues and to take their place in the neuromuscular field. Moreover, three new mentees were selected to join the Mid-Career Mentoring Programme and be accompanied by experienced mentors. Now in total seven mentees benefit from this ENMC Programme and we expect more to come in the next submission round of 1 July 2023.

ENMC also welcomed two international patient federations, the World Duchenne Organisation and SMA Europe, who joined as Associated Partners, reinforcing the link between ENMC and patient communities around the world.

None of this would have happened without the commitment and support of every member of the ENMC community. Therefore, I would like to extend my warmest thanks to the team in Baarn, the members of the Research Committee and Executive Committee, the Associated Partners, the workshop organisers and participants and the Company Forum for their supporting contributions.

Dr Alexandre Méjat,
Chair of the Executive Committee
Representative of AFM Telethon, France

2 ENMC has lived its mission for more than over 30 years

History of ENMC

In 1988, parents of children affected by neuromuscular conditions and top-level clinical researchers working on these rare diseases came together to tackle the question: "how can we speed up the discovery of treatments for patients with these devastating diseases?"

At that time there was a lot of fragmentation of research, making it difficult to perform trials on rare diseases with just a handful of patients in each country. The most important step was to start international communication and collaboration. The group, driven by a few European patient organisations, decided that the answer to the above question was to bring the neuromuscular experts from all over the world together.

Therefore, the European Neuromuscular Centre (ENMC) was founded in 1992 to organise small-sized scientific meetings over a weekend, facilitating research discussions, sharing of unpublished data and exchanging ideas for the future.

ENMC Mission Statement

The mission of ENMC is to encourage and facilitate communication and collaboration in the field of neuromuscular research with the aim of improving diagnosis and prognosis, finding effective treatments and optimising standards of care to improve the quality of life of people affected by neuromuscular disorders.

"Connecting people"

Over the years, patients and their representatives were invited to bring their perspective and needs to the workshop discussions. Each workshop group was asked to deliver a well-thought plan for the future and demonstrate the commitment to work together. The ENMC was installed to finance but also to organise these international workshops, relieving the workshop organisers from operational tasks. The staff has now grown to six part-timers who coordinate all ENMC activities. The ENMC office is located in the building of Spierziekten Nederland, in Baarn, The Netherlands.

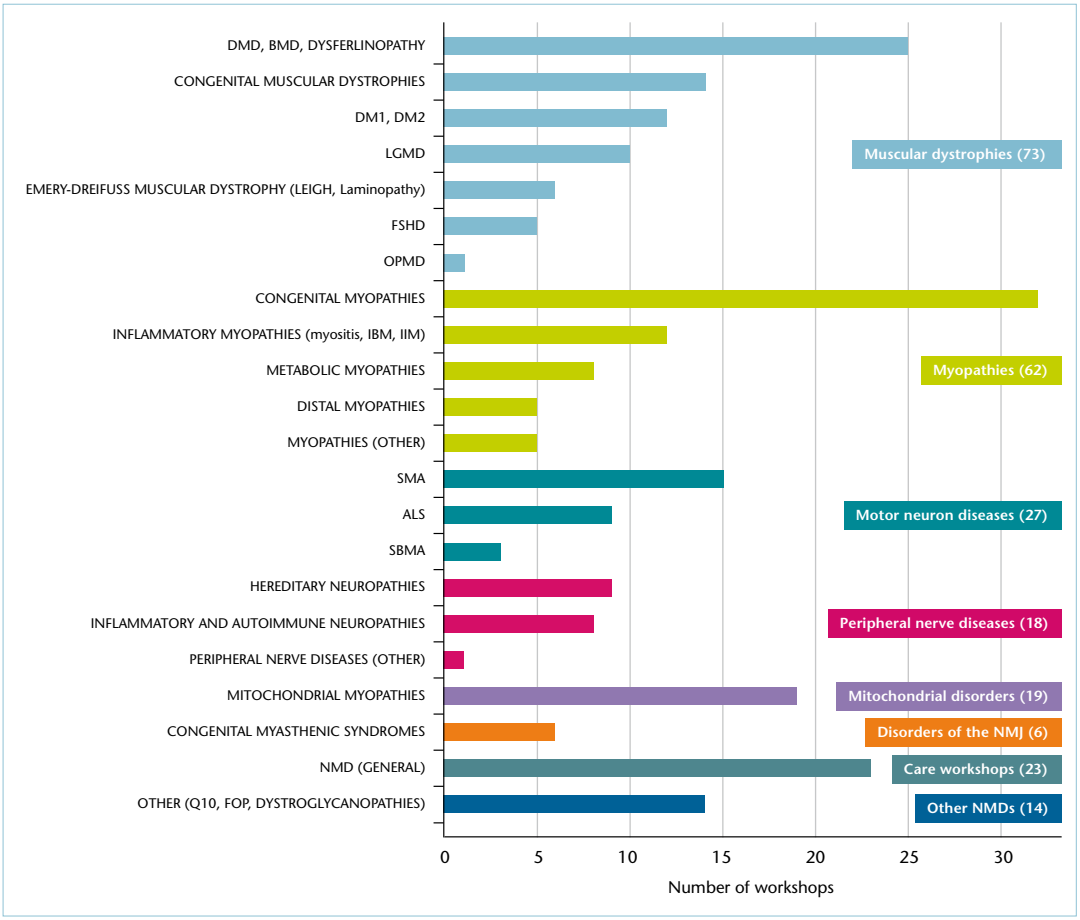
What was the impact of 30 years' ENMC workshops?

In the first decade, the workshops were predominantly dedicated to understanding the molecular and genetic causes of neuromuscular conditions, the first step to a right diagnosis and to make drug development possible (this is called basic research).
In the second decade, the topics focused on the next phase of research: animal models, biobanks and registries. In general, here the most important question was: how to bring the research from the lab bench to the patient bed (so-called translational research)? Ten years ago, the first trials in patients were started, so many ENMC workshops focused on the design of these trials and on the definition of outcomes measures that are relevant for the researchers and for the patients (this is called trial readiness). The ENMC highly values the involvement of patients in the trial readiness workshops. Several consortia have evolved successfully over the years and have developed treatment guidelines for patients with neuromuscular conditions. Today, strong innovations like gene therapy are being tested for some neuromuscular conditions, and the first drugs are becoming available for patients. However, some less frequent diseases still need collaborations and discussions on basic research and translational research topics.
The ENMC strives to offer an international platform for communication also for these conditions.

In 30 years the ENMC accomplished to:

- Promote discussion about more than 30 different rare neuromuscular conditions (see graph on the next page).
- Create over 30 consortia of experts dedicated to these neuromuscular conditions, and who have continued working together for decades.
- Organise more than 270 ENMC workshops (on average 9 workshops per year).
- Establish a network of over 4500 participants from more than 75 countries and from 5 continents.
- Publish 270 lay reports on our website (www.enmc.org) and over 220 full papers in the journal Neuromuscular Disorders with a high average citation score of 1,24.
- Engage patients in ENMC activities and introduce them to our international network. We welcome and proactively invite patients and patient representatives with experience in medical science meetings to our workshops. Preparatory meetings are set-up to explain the essence of the workshop, bring patients in contact with the organisers and facilitate that they can bring the patient's voice to the workshops. See also: https://www.enmc.org/patient-participation/.
- Empower the next generation of clinicians and scientists in the neuromuscular field by two inspiring programmes. Early career researchers can apply for a seat in one of our workshops and mid-career researchers can request for individual mentoring by established leaders.
- Set up the Themed Workshop Call which is intended to cover strategic and transversal topics, which are relevant to a wide range of neuromuscular conditions (see grey bar below), such as ventilation, cardiomyopathy, pregnancy, exercise, Newborn Screening, Covid-19 etc.

Neuromuscular conditions topic of discussion at ENMC workshops (1992-2023)*



*Neuromuscular conditions topic of discussion at ENMC workshops (1992-2023) (Source NMD classification: Muscular Dystrophy UK and Prinses Beatrix Spierfonds, the Netherlands). This figure illustrates the number of times a disease class was topic of an ENMC workshop in the last 30 years, e.g. muscular dystrophies were the most frequently discussed disease types (73 times) in 30 years' time with almost 30 workshops dedicated to Duchenne muscular dystrophy. This was closely followed by the Myopathies with 63 workshops. If multiple neuromuscular diseases were covered in one workshop, this workshop was addressed as a "NMD General" workshop. In such a workshop, a common topic important for multiple NMDs was addressed, such as standards of care, ventilation or management of pain, fatigue or psychological problems. Abbreviations: ALS = amyotrophic lateral sclerosis; BMD = Becker muscular dystrophy; DM1 or DM2 = myotonic dystrophy type 1 or 2; DMD = Duchenne muscular dystrophy; FOP = fibrodysplasia (myositis) ossificans progressiva; LGMD = limb girdle muscular dystrophy ; NMD = neuromuscular disorder; NMJ = neuromuscular junction; OPMD = oculopharyngeal muscular dystrophy; Q10 = co-enzym Q (ubiquinone)-10; SBMA = spinal bulbar muscular atrophy; SMA = spinal muscular atrophy.

Heading for the future!

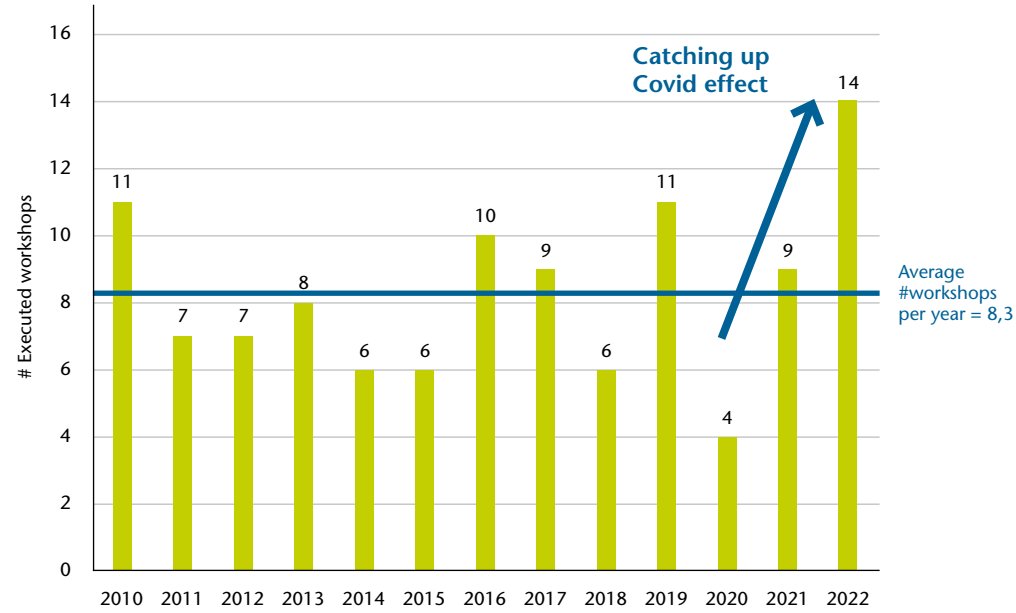
We are in the middle of a fast-changing landscape with new players on board, like the pharmaceutical industry, small biotechnology companies, the regulatory authorities, health economics and many more. The ENMC is driven by the needs of the patient and the science community and we aim to stay in the centre for at least another 30 years! We strive to continue bringing experts and patients together to jointly work on future improved diagnosis, successful treatments and care for neuromuscular patients.

3 The ENMC workshops in 2022

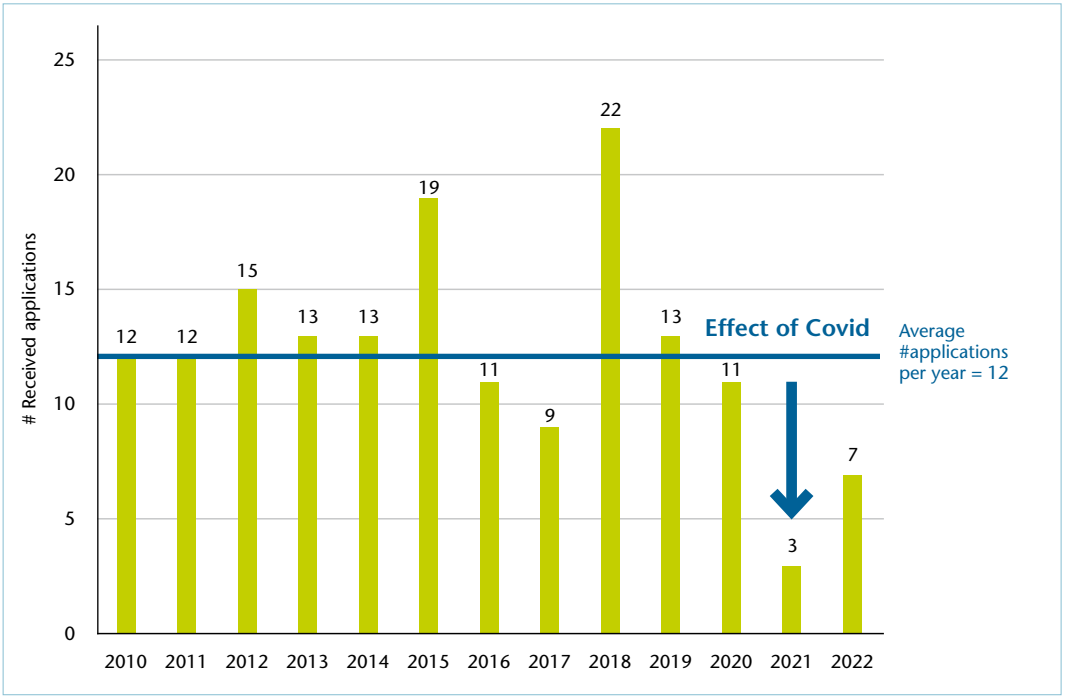
Many ENMC workshops that were planned to take place in 2020 were postponed to 2021 due to outbreak of Covid-19. But again in 2021 the pandemic prevented the ENMC from organising face-to-face workshops in the Courtyard Marriott Hotel, Hoofddorp, The Netherlands and our hopes were for 2022. This year, we organised 14 workshops (see table in section 3.2), most if not all were in a hybrid form. The reason why ENMC could not yet return to face-to-face meetings, was because many workshop participants were still restricted in travelling due to Covid-19 infection or vulnerability, CO2 emission policies of institutes, and other valid reasons. ENMC set up a professional hybrid meeting to accommodate these participants in attending the workshops online. Audiovisual performance was of top quality as indicated by many workshop organisers.

We are extremely grateful to members of the ENMC team who were able to manage this busy schedule in 2022.

Covid pandemic impact on the number of executed workshops



Covid impact on the number of received workshop applications



In 2022 seven workshop applications were submitted, of which one was a re-application. Five of these applications were selected for financing by the ENMC, two already took place in 2022 and three are planned for 2023.

3.1 Themed workshops

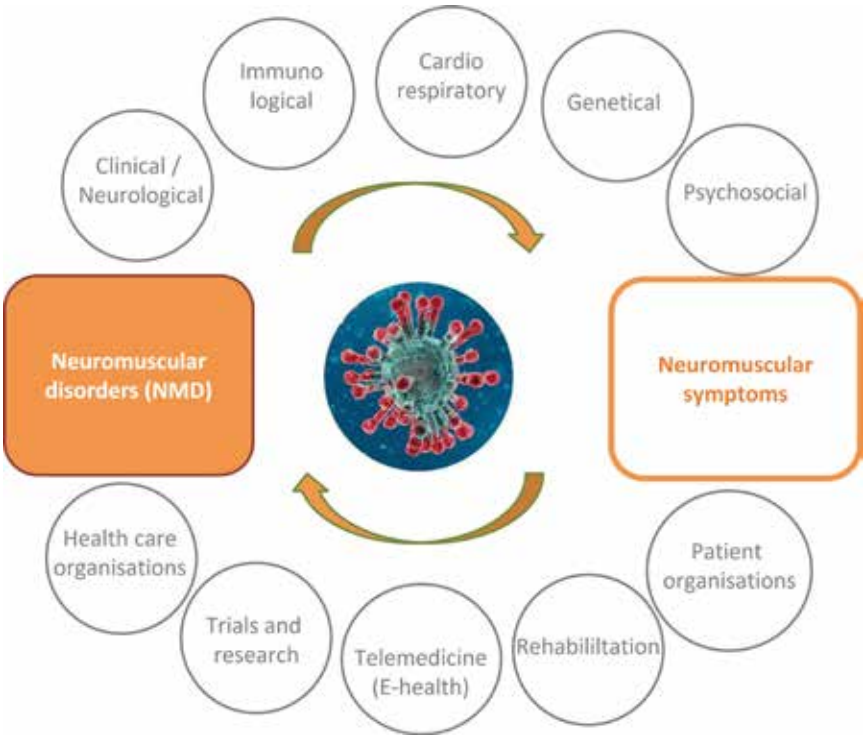
THEMED WORKSHOPS

In addition to the regular ENMC workshop applications, where topics of the workshops originate from the workshop organisers, ENMC launched a call for themed workshops applications. This programme was set up to prepare the stepping-stones for the future by listening to the needs of neuromuscular patients and the research community. With a "Themed Workshop Call", the ENMC provides workshop funding opportunities for one or two themed workshops per year, focusing on a pre-identified topic which:

- Is of broader interest to more than one condition (transversal workshops).
- Requires a multidisciplinary approach.
- Is not often discussed in a meeting.
- Is groundbreaking and strategic and requires the development of a sustainable platform in the future.

In 2021, the chosen theme for a Themed Workshop in 2022 was:

Post-Covid-19: Issues and opportunities for the neuromuscular field
Learning experiences from the Covid-19 pandemic regarding neurological, psychological, immunological, social, economic, technical etc. aspects for neuromuscular patients in self-isolation and Corona-virus infected people who developed neuromuscular symptoms.



The call resulted in the approval of a workshop application entitled: "Remote delivery of clinical care and validation of remote clinical outcome assessments in neuromuscular disorders: a response to Covid-19 and proactive planning for the future."

New themes will be chosen by the ENMC for future years and will be announced to the community in Q2 2023. People from the neuromuscular field are encouraged to pick up one of these themes and apply for a Themed Workshop (submission deadline is 1 March 2024). Those applications which will be selected by the ENMC in April 2024 are planned to be organised as workshops in 2024 or 2025.

3.2 Summary of ENMC workshops held in 2022

Workshop no./date and format	Topic	Workshop leaders
Workshop no. 254 28-30 January 2022 (virtual)	Formation of a European network to initiate a European data collection, along with development and sharing of treatment guidelines for adult SMA patients	Prof. P. Laforêt, Dr E. Pegoraro, Dr L van der Pol, Prof. M. Walter
Workshop no. 262 11-12 February 2022 (virtual) 4 July 2022 (face-to-face)	Standards of Care for the Dysferlinopathies	Prof. V. Straub, Dr A. Mayhew, Dr T. Stojkovic, Dr L. Bello
Workshop no. 260 11-13 March 2022 (hybrid)	Congenital Myasthenic syndromes	Prof. L. Maggi, Dr P. Rodriguez-Cruz, Dr D. Beeson, Prof. H. Lochmüller
Workshop no. 258 25-27 March 2022 (hybrid)	Genetic Epidemiology and Clinical Trial Readiness in Encephalomyopathy of Leigh Syndrome	Prof. E. Bertini, Prof. S. Rahman, Prof. B. Cohen, Prof. M. Schiff
Workshop no. 266 1-3 April 2022 (hybrid)	Remote delivery of clinical care and validation of remote clinical outcome assessments in neuro-muscular disorders: a response to Covid-19 and proactive planning for the future	Dr L. Lowes, M. James, Dr L. Alfano, Dr G. Ramdharry
Workshop no. 265 22-24 April 2022 (hybrid)	Muscle Imaging in Facioscapulohumeral Muscular Dystrophy (FSHD): relevance for clinical trials	Dr G. Tasca, Dr S. Attarian, Prof. J. Vissing, Prof. J. Díaz Manera
Workshop no. 263 13-15 May 2022 (hybrid)	Focus on female carriers of dystrophinopathy: refining recommendations for prevention, diagnosis, surveillance and treatment	Prof. A. Ferlini, Dr J. Bourke, Dr R. Quinlivan, Dr A. Sarkozy
Workshop no. 267 20-22 May 2022 (hybrid)	Psychological Interventions for improving quality of life in slowly progressive neuromuscular disorder	Dr N. Voet, Dr C. Graham, Dr B. Gallais
Workshop no. 257 10-12 June 2022 (hybrid)	The 3rd ENMC workshop on Dystroglycan and the Dystroglycanopathies	Prof. S. Winder, Prof. V. Straub, Prof. K. Campbell
Workshop no. 261 17-19 June 2022 (hybrid)	Management of safety issues arising following AAV gene therapy	Prof. I. Servais, Prof. F. Muntoni, Prof. C. Bönnemann
Workshop no. 253 24-26 June 2022 (hybrid)	Skeletal muscle laminopathies - natural history and clinical trial readiness	Dr G. Bonne, Dr L. Maggi, Prof. S. Quijano-Roy, Prof. C. Bönnemann
Workshop no. 255 9-10 September 2022 (hybrid)	Muscle imaging in Idiopathic Inflammatory Myopathies	Prof. M. de Visser, Prof. J. Vencovský, Dr P. Carlier
Workshop no. 268 30 Sept-02 October 2022 (hybrid)	Genetic diagnosis, clinical classification, outcome measures, and biomarkers in FSHD: relevance for clinical trials	Dr N. Voermans, Dr R. Lemmers, Dr K. Mul, Dr J. Dumonceaux
Workshop no. 269 9-11 December 2022 (hybrid)	Clinical trials in DMD: Ten years on, what have we learned? How can we optimize future trial design?	Prof. F. Muntoni, Prof. N. Goemans, Prof. C. McDonald, Prof. E. Mercuri

Note: The workshop number (no.) is given once an application is officially approved and hence dates can be reserved. It does not always precisely reflect the timing of the execution of the workshop.

254th ENMC International workshop: Formation of a European network to initiate a European data collection, along with development and sharing of treatment guidelines for adult SMA patients

Background

Compared to drug therapies in common diseases, approval of orphan drugs is often based on a limited amount of evidence. But to evaluate the long-term effect of these drugs in a broad spectrum of patients, it is crucial to collect clinical data on the respective patients systematically, following the FAIR principles of data (findable, accessible, interoperable, reusable). Harmonisation of existing international SMA registries is needed to speed up the identification of characteristics, biomarkers and genetic modifiers that predict the effects of drug treatment in different subgroups of SMA patients. Additionally, the relative lack of natural history data of adult SMA patients complicates interpretation of treatment effects.

Aims of the workshop

The workshop aimed at creating a European network to initiate a European data collection, the development and sharing of treatment guidelines for adult patients affected by SMA and the discussion of relevant aspects of current and future SMA therapy, real-world evidence, mode of treatment application, biomarkers, and start/stop treatment criteria.

Workshop deliverables

The group agreed on common denominators for a harmonized data collection; a realistic phenotype-related minimal dataset for patient follow-up, with different tests for different types of patients affected by SMA; and drafted a consensus draft protocol for monitoring treatment safety and efficacy.

Additionally, specific recommendations for the transition of SMA patients from paediatric to adult care were agreed upon.

Participants of workshop 254 in the Zoom room.

262nd ENMC International Workshop: Standards of Care for the Dysferlinopathies

Background

Dysferlin-related Limb Girdle Muscular Dystrophy (LGMD R2) is a slowly progressing muscular dystrophy. Dysferlinopathy patients report long delays to diagnosis and mixed experiences of access to meaningful care. In the absence of approved treatments, care by the multidisciplinary team is key to maximising quality of life. Low prevalence of dysferlinopathy necessitates expert advice on management being collated on an international level. With the upcoming of international, multi-center clinical trials for this rare condition, variation between care providers need to be minimised.

Aims of the workshop

The major aim of this ENMC workshop was to assemble international experts in dysferlinopathies to develop care guidelines and standardise them between centres, based on the natural history data collected since 2012 by the Clinical Outcome Study (COS) in dysferlinopathy.

Workshop deliverables

- An algorithm for diagnosis of dysferlinopathies for non-experts.
- Recommendations for care and management of the disease.

An initial virtual session focused on the dissemination of the COS results, after which working groups were formed to focus on the following main topics:

1. Diagnostics and genetics.
2. Motor function and exercise.
3. Cardiac, respiratory and considerations for emergency and surgical care.
4. Pregnancy, immunological, endocrine and nutritional considerations.

The working groups developed recommendations, which were further refined at the face-to-face meeting. The group will now work on publishing the care guidelines and on embedding them in routine practice.

Participants of workshop 262 on Dysferlinopathies met each other face-to-face in Brussels linked to ICNMD in July 2022.

260th ENMC International Workshop: Congenital myasthenic syndromes

Background

Congenital myasthenic syndromes (CMS) are inherited disorders in which neuromuscular transmission is compromised by various genetic defects of neuromuscular junction proteins and, in some instances, of more widely expressed glycosylation genes. Since the last ENMC workshop on CMS in 2011 (186th workshop), additional CMS genes have been identified through next-generation sequencing. This led to the development of new therapeutic approaches such as AAV gene therapy and Muscle-Specific Kinase agonist antibody therapy showing promising results in animal models. However, the scarcity and diversity of this rare condition poses challenges for clinical trial design, planning and recruitment. Therefore, a group of CMS experts came together in an ENMC workshop to upgrade the current state-of-the-art knowledge on CMS and define the next steps for international research.

Aims of the workshop

1 Review insights from preclinical studies and define strategies to develop new treatments in CMS.
2 Share available data on natural history in adult and paediatric CMS.
3 Establish clinical and non-clinical outcome measures that could be adopted to provide consistency across different centres and clinical trials.

Workshop deliverables

The workshop participants discussed the underlying CMS pathophysiology, animal models, current and future approaches to diagnose and treat CMS patients. They are often responsive to treatment with different, already available medications, but early and correct diagnosis remains challenging. To aid novel CMS gene discovery and improve diagnosis, comparison and sharing of laboratory samples and clinical protocols are needed.

A large part of the meeting was devoted to outcome measures, and it was recommended that these should be tailored to underlying clinical patterns and genes. Other suggestions included examining the minimal clinically important difference in outcome

Dr Andreas Roos and Prof. Hanns Lochmüller during workshop 260 on Congenital Myasthenic syndromes at the Courtyard Marriott Hotel, Hoofddorp, The Netherlands.

measures that can be applied in telehealth sessions, examining 'wearable digital devices', and looking at outcome measures used in previously conducted and successful clinical trials in myasthenia gravis, including patient-reported-outcome-measures. The awareness and understanding for CMS among health care professionals and the lay public requires further attention. The importance of collaborations with patient organisations was stressed as this would increase the impact of research, by getting more patient data into databases and understanding the natural history of CMS. Furthermore, this collaboration aims to spread information, create lay friendly questionnaires, and prepare education programmes.

258th ENMC International Workshop: Genetic epidemiology and clinical trial readiness in encephalomyopathy of Leigh Syndrome spectrum (LSS)

Background

Leigh syndrome, also known as a "subacute necrotizing encephalomyopathy", is a genetically heterogeneous disease that primarily affects the central nervous system. This brain condition usually affects young children (adult onset is very rare) and is caused by a variety of different genetic problems. Originally described in 1951 by Dr Denis Leigh, this syndrome typically involves damage to the basal ganglia, thalamus, brainstem and spinal cord.

Aims of the workshop

The aims were to increase knowledge of the natural history of Leigh syndrome, to improve its diagnosis, to collect information on the genetic epidemiology of the syndrome, to facilitate the identification of biomarkers, and to move forward with possible therapeutic strategies.

Workshop deliverables

- An international collaborative project collating clinical and imaging features of non-primary mitochondrial disease causes of LSS.
- The potential use of a shared imaging protocol across multiple international centres and plans for delivering the Leigh Syndrome Roadmap Project (LSRP).
- A prospective natural history study.

Genetics of LSS were discussed and updates were provided on several ongoing genomic projects and LSS registries from Italy, UK, USA, France, Czech Republic, Australia and Japan. A review of biomarkers for primary mitochondrial diseases was given.
An overview was given about modelling LSS in patient-derived brain organoids and on pharmacological screening of repurposed drugs in induced pluripotent stem cells (iPSCs) also derived from patients affected by LSS. Repurposed drugs are drugs licensed for a different purpose but now investigated for potential use in mitochondrial disease. Finally, ways to engage with the European Medicines Agency to take forward potential compounds into a formal clinical trial for LSS was discussed.

The patient perspective

Faye Wylie (Leigh Network, UK) gave a moving account of the lived experience of Leigh syndrome through childhood into adult life and recited a poem written by herself. Patient registries from the Patient Advocacy Group viewpoint were presented and MitoSHARE was introduced: a global research database with multi stakeholder oversight.
The importance of multidisciplinary collaboration and lessons learned from the Duchenne muscular dystrophy experience was emphasized by the LSS patient representatives.

A poem that describes the lived experience by Faye Wylie (UK).

BATTERY OF LIFE

Imagine you are a mitochondrion
A pocket of energy powering the body
Run, run, run
Power, power, power
Mi-to, mi-to, mi-to
Must reach brain, must reach heart
must reach muscles
Pedal, pedal
Faster, faster
Climb to the eyes
This mountain is so high
Flash, flash
Low battery, low battery
Reserve, reserve, reserve
Important organs only
A power cut has occurred
A power cut has occurred
A power cut has occurred
Reserve what we can
Body in failure

Onsite and online participants of workshop 258 on Leigh Syndrome.

The organisers of Workshop 258, Prof. E. Bertini, Prof. S. Rahman, Prof. B. Cohen and Prof. M. Schiff, all agreed:

"These virtual and hybrid ENMC meetings have been an excellent opportunity to update and deepen our knowledge of the genetic causes and natural history of Leigh syndrome, promoting international research and collaborative studies, including fruitful discussions about prospective natural history studies and clinical trials."

266th ENMC International Workshop: Remote delivery of clinical care and validation of remote clinical outcome assessments in neuromuscular disorders: a response to Covid-19 and proactive planning for the future

Background

Standardised assessments of muscle strength and function are used to track disease trajectory. This is needed to prospectively advise the need for equipment, home and work modifications, and other assistive devices in individuals with neuromuscular disorders (NMD). Clinical outcome assessments (COA) of strength and function are often primary or secondary endpoints for pharmacological, rehabilitation interventions or natural history studies. It is critical that data representing key functional endpoints are obtained via highly controlled and standardised procedures by individuals who are qualified and adequately trained to collect them.

The Covid-19 pandemic presented unprecedented challenges to the in-person delivery of clinical care and clinical trials. A fast response and alternative strategies to in-person clinic-based assessments were required to protect study efficacy endpoints and ensure ongoing patient evaluations. A group of expert physiotherapists in NMD, working across clinics, countries, and clinical trials developed initial guidelines for the suitability and feasibility of performing COA commonly used in clinical trials.

Aims of the workshop

The major aim of this workshop was to evaluate the utility and validity of conducting remote clinical outcomes assessments for NMD.

Workshop deliverables

1. Documentation of remote clinical health assessments for care or treatment of NMD patients, clinical studies underway and natural history studies.
2. Sharing of data from prospective studies evaluating the validity and reliability of remote testing of COA.
3. Standardised training of COA and e-health capacity building.

Patient, researcher and sponsor experience of remote clinical and research assessments was shared. Statistical considerations for the comparison of clinic and at home data were reviewed along with the important current and future potential roles of patient registries. The current state of standardised training of COA in clinical trials around the globe was reviewed. Adaptions to remote delivery of health care and lessons learned were discussed. The group highlighted the challenges in global e-health including new parts of the world while respecting and carefully navigating cultural differences.

This was an excellent example of an ENMC Themed Workshop. The overall aim of these meetings is to open up discussions among relevant experts from all over the world focusing on a common problem or topic applicable to a wide range of neuromuscular disorders. Topics which have a great impact on the daily work of health care professionals and researchers and on the quality of life of patients and families affected by NMDs are ideal contents for an ENMC Themed workshop.

A coffee break during workshop 266 for further discussions, with from left to right Lindsay Alfano, Meredith James, Alexandre Méjat and Gita Ramdharry.

265th ENMC International Workshop: Muscle imaging in facioscapulohumeral muscular dystrophy (FSHD): relevance for clinical trials

Background

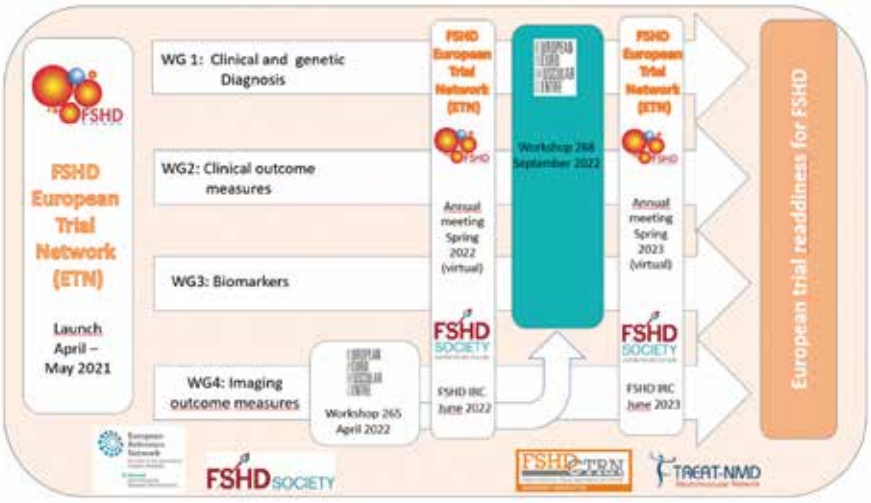
Facioscapulohumeral muscular dystrophy (FSHD), one of the most frequently occurring muscular dystrophies, is at the doorstep of clinical therapeutic trials. The scientific community is committed to reach clinical trial readiness, and two major consortia devoted to boost drug development have been created (the FSHD Clinical Trial Research Network (CTRN), based in the US and more recently the FSHD European Trial Network, ETN). Notably, FSHD is unique in its genetic mechanism and very peculiar in the progression of muscle damage compared to the other muscular dystrophies.

Muscle imaging through magnetic resonance (MRI) has lately been established as an important tool to diagnose and follow the evolution of different neuromuscular disorders. In FSHD, evidence derived from MRI studies substantially contributed to a better understanding of this disease and of its variable progression over time.

Aims of the workshop

To establish the importance of muscle imaging techniques for the diagnosis and follow-up of FSHD patients, and to define the role of MRI in a clinical trial setting. No previous meeting has been specifically devoted to address these issues.

The FSHD European Trial Network (ETN) was established in 2021 with the aim to connect the clinicians involved in care for FSHD in all European countries and increase the trial capacity in Europe allowing more centres to participate in upcoming trials and making new treatments widely accessible to patients. A mission which fits very well in the scope of the ENMC. Therefore the ETN consortium used the ENMC workshop platform to bring all relevant stakeholders together this year following the process for two separate applications. Four ETN workgroups were formed in 2021: WG1 would deal with clinical and genetic diagnosis, WG2 with clinical outcome measures, WG3 with biomarkers for FSHD and WG4 with imaging outcome measures. WG1-3 came together in an ENMC workshop (#268) in September 2022 which will be highlighted later in this impact report. In the MRI workshop described here (#265), participants of WG4 came together in April 2022. See picture on the next page published with consent from Dr Nicol Voermans, coordinator of the ETN.



Workshop deliverables

As a preparatory activity of the workshop, a survey of the imaging facilities (MRI, ultrasound) available at each participating centre and used for evaluation of FSHD was disseminated and the results were part of the deliverables. The following imaging tools to use in FSHD were discussed:

- Qualitative MRI.
- Quantitative MRI.
- Muscle Ultrasound.
- MRI techniques used in clinical trials.
- Correlation with functional outcomes and other imaging techniques.

The participants agreed on the diagnostic usefulness of MRI in particular contexts, and on its role in patients' stratification to enter a clinical trial.

Ultrasound expertise is currently restricted to specific centres, but if standardised in multiple sites, it could help in providing additional information to MRI also in a clinical trial framework.

Concerning quantitative MRI, efforts should be made to harmonise and improve protocols that had been already implemented in previous trials. Researchers should aim to achieve whole-body coverage given the heterogeneity and unpredictability of FSHD, as well as to include specific sequences to assess disease activity. The idea to tailor the choice of the specific imaging biomarker(s), based on the action of the investigated drug, also clearly emerged.

Coordination with the imaging working group already in place in the CTRN is mandatory to optimise efforts, and joint meetings, both online and live, will be arranged for this purpose.

All participants attending the workshop 265 on muscle imaging in FSHD.

263rd ENMC International Workshop: Focus on female carriers of dystrophinopathy: refining recommendations for prevention, diagnosis, surveillance and treatment

Background

Females who carry a DMD gene mutation can present with a spectrum of features: the majority of female carriers show no symptoms or no abnormalities on blood or cardiac testing, some have no symptoms but have a raised blood creatine kinase level, some develop cardiomyopathy, and some may develop muscle pains and/or muscle weakness. In some women muscle weakness and cardiac features can have a significant impact upon quality of life. How best to manage women presenting with symptoms is not clear due to the lack of both natural history data and dedicated research.

Aims of the workshop

This workshop was convened to understand what is already known from research and what the gaps might be. In addition, the care needs of women presenting with symptoms were discussed and consensus recommendations included the need for a multidisciplinary approach to care management. Experts covering a range of specialties from across Europe and the USA discussed the terminology, diagnosis, clinical features and impact of skeletal and cardiac manifestations in women carrying pathogenic variants (mutations) in the DMD gene. The workshop also reviewed the implications for medical care including cardiac surveillance.

Workshop deliverables

- Discuss the nomenclature and select the best terms.
- Determine whether the degree of X chromosome inactivation is a valuable predictor of symptoms.
- Increase awareness in patient families and health care professionals of the potential for developing symptoms, especially in muscle and/or heart, amongst women who carry a DMD gene mutation.
- Define the role for psychologists in assessing cognitive problems due to dystrophin deficits in the brain of female carriers.

Several recommendations for female DMD carriers were agreed upon:

- The name “manifesting carrier” is not helpful and should be changed to reflect the clinical picture. The term ‘carrier of a DMD gene mutation’ should be reserved to indicate a female carrying a DMD gene mutation who is asymptomatic and with normal investigations. For females in whom there is evidence of clinical involvement (signs or symptoms), the term ‘female patients with dystrophinopathy’, including ‘female patients with muscular dystrophy and/or cardiomyopathy caused by dystrophinopathy’, could be reserved. Future will learn how the nomenclature will be adopted in the NMD field.

- The minimum care standards should include full genetic testing of all potential female carriers. If a mutation is confirmed, the carrier should be referred to a neuromuscular and cardiology specialist for further assessment.

- Advocacy groups could be particularly helpful in achieving awareness about this condition among DMD patient families globally.

- It was agreed that international research collaborations are critical to improving care and treatment standards for affected females. This may include the development of patient registries and natural history studies leading to robust outcome measures for clinical trials and research funding applications.

Participants of the 263rd ENMC International Workshop on female carriers of dystrophinopathy.

267th ENMC International Workshop: Psychological Interventions for improving quality of life in slowly progressive neuromuscular disorders

Background

Having a diagnosis of a neuromuscular condition (NMD) may impact the psychosocial functioning of people living with the condition. The literature emphasises that psychological treatments targeting psychosocial factors have the potential to improve quality of life, mood, and functioning with pain and fatigue in NMD. At this moment, in many countries and centres psychological interventions are not yet embedded as a standard in the routine clinical care offered to people living with NMD. Harmonisation of these guidelines and individual approaches are warranted.

Aims of the workshop

The aim of the workshop was to develop international guidelines for psychological interventions which may improve quality of life in patients affected by slowly progressive NMD, their family members and caregivers. The workshop aimed to bring together experts in psychology and cognitive behavior in NMD to share research, clinical and personal experience.

Prior to the workshop, organisers, expert patients, and early career researchers developed a questionnaire for NMD patients, caregivers, and professionals. This sought to collect opinions on the critical psychosocial needs in NMD, how psychological support should be configured, and the barriers to accessing psychological interventions. The survey outcome showed that those affected by NMD consider psychological support necessary for physical (loss of function, pain, and fatigue), social (changing relationships, stigma), and psychological (fear, shame, accepting the disease, feelings of guilt about hereditary diseases) problems. Close relatives can have trouble coping with the disease of their child, parent, or partner and its impact on daily life responsibilities, such as family and work.
The professionals who completed the questionnaire mentioned the importance of communication between the multidisciplinary team and patients and their close relatives in all stages of NMD.
The presence of a mental health professional within the multidisciplinary team is a must.

Although the need for psychological support was evident, respondents described many barriers to accessing psychological support such as unpleasant feelings of shame, fear or self-sufficiency, followed by logistical and financial issues.

Discussions in the workshop 276 were continued outside the meeting room.

The patient's voice was well covered in workshop 267 by Ms Ingrid de Groot and Mr Marnix van Bruggen.

Workshop deliverables

- Recommendation that psychological interventions should be embedded in the routine clinical care offered to people living with NMD, both for the patients and their families/caregivers.
- Recommendations to reduce the barriers to participating in psychological support.
- Creation of a consortium, which will continues haring up-to-date evidence and best clinical practice and promote collaboration on research programmes related to psychological support in NMD.

257th ENMC International Workshop: The 3rd ENMC workshop on Dystroglycan and the Dystroglycanopathies

Background

Dystroglycan is a core and essential component of the dystrophin-glycoprotein complex of muscle and brain cells, making vital links between the cytoskeleton and the protein laminin in the extracellular matrix. Perturbations in the ability of dystroglycan to interact with laminin have severe implications for muscle function. These diseases have collectively been termed dystroglycanopathies. A heightened clinical awareness of the spectrum of these diseases coupled with greater use of DNA and protein sequencing has led to the identification of several new genes involved in dystroglycan synthesis, particularly its glycosylation, and other pathways relevant for dystroglycan function. There are nevertheless several incompletely understood aspects of this group of disorders. Indeed, pathologies range from relatively mild late-onset muscular dystrophy, to perinatally lethal severe muscular dystrophy with significant neurological abnormalities.

Onsite and online participants of workshop 257 on Dystroglycan and Dystroglycanopathies.

Aims of the workshop

The aim of the workshop was to bring together researchers working on the modification of dystroglycan, so they could discuss the involvement of this protein in the pathophysiology of dystroglycanopathies. In addition, natural history and epidemiology data for dystroglycanopathies and clinical trial plans were addressed.

Workshop deliverables

- A greater appreciation of how disease mechanisms can lead to the identification of new treatment modalities and therapeutic interventions.
- Identification of knowledge gaps or shortcomings in tools (models) to study basic and preclinical aspects of the dystroglycanopathies.
- Potential reconciliation of the genotype with phenotype conundrum and how we use this information therapeutically.

261st ENMC International Workshop: Management of safety issues arising following AAV gene therapy

Background

Adeno-associated viral (AAV) gene therapy approaches have the potential to fundamentally change treatment paradigms for several neuromuscular diseases, with the most advanced example provided by spinal muscular atrophy (SMA) for which the AAV9-SMN therapeutic (onasemnogene abeparvovec, Zolgensma©) has received regulatory approval, is commercially available in many countries and has been given to more than 2000 patients.
A number of other AAV gene therapy products are at various stages of clinical development, including in X-linked-myotubular myopathy, limb girdle muscular dystrophy, Pompe disease and Duchenne muscular dystrophy, as well as other rarer neuromuscular conditions.

While progress in the development of these products has been striking in the last few years, the field has also seen the emergence of sudden unexpected serious adverse reactions (SUSAR) that tragically led to the death of some study participants. Over time, and with more patients having received AAV therapies for different conditions, different patterns of such adverse events have emerged. Now it is time to bring all this knowledge together, share experiences and prepare international guidelines about what SUSARs are documented and can be expected from AAV-mediated gene therapy in NMD and how to manage them.

Aims of the workshop

The workshop was devoted to review reports, characterizations and management of emerging adverse events related to the use of adeno-associated viral gene therapy vectors for neuromuscular disorders, including those in clinical trials and in approved commercial use.

Workshop deliverables

1. Draft guidelines for how to monitor patients after gene therapy administration.
2. Draft guidelines for appropriate prevention measures prior to gene therapy administration.
3. Draft guidelines on identification of individuals especially susceptible to SUSARs.
4. Draft guidelines for management of side effects following gene therapy.

One of the conclusions of the workshop discussions is that the different aspects of potential toxicity result from a complex interface between the AAV virus, the transgene used, the specific condition and the specific genotype of the individual patients and their immune status to the AAV capsid and to the transgene. But also underlying co-morbidities and previous exposure to other infective agents are involved in a complex interplay that is only starting to become understood.

The participants agreed that this workshop is addressing a timely need, namely, to allow AAV mediated gene therapy to proceed safely with procedures in place to anticipate and manage emerging complications. A number of future collaborative options were discussed, ranging from registries of patients treated with these therapies, especially if coupled with genomic data, to multi-sponsor collaboration on class specific adverse events observed across a number of different conditions, to the establishment of more clear protocols for surveillance and management of the more common adverse events.

Participants of the 261st ENMC International Workshop on AAV gene therapy.

253rd ENMC International Workshop: Skeletal muscle laminopathies (SML) – natural history and clinical trial readiness

Participants of the 253rd ENMC International Workshop on Skeletal muscle laminopathies (SML) in the meeting room.

Background

Skeletal muscle laminopathies (SML) are rare hereditary human diseases which are linked to mutations in genes encoding proteins of laminin, a structure in the nucleus of skeletal cells. They are characterized by skeletal and cardiac muscle involvement, metabolic disorders and premature aging syndromes.

The last ENMC international workshop on laminopathies was held in 2007, and many achievements have been reached in the last decade. In particular, progress has been made in the knowledge of natural history and pathophysiology, raising the need of an update on topics discussed up till now.

Aims of the workshop

1 To share available data on natural history in adult and pediatric SMLs among experts.
2 To create working groups focused on the identification of clinical outcome measures and biochemical, molecular and imaging biomarkers useful for natural history studies and future clinical trials.

Workshop deliverables

The workshop allowed substantial and productive discussions and ended with propositions for further developments of preclinical research, including deeper understanding of pathological mechanisms at play and development of therapeutic approaches, as well as for starting prospective natural history studies. These are deliverables which are all necessary for complete clinical trial readiness for SML. According to patient voices and needs, it was agreed to prepare care guidelines for management of cardiac and non-cardiac features in patients with SML with support from the European Reference Network Euro-NMD. Also, a shared international platform gathering updated information with easy access for every patient and their families will be set up. Finally, the French patient registry named "OPALE" will be upgraded towards an European/International patient registry.

255th ENMC International Workshop: Muscle imaging in Idiopathic Inflammatory Myopathies

Onsite and online participants of the 255th ENMC International Workshop on muscle imaging in Idiopathic Inflammatory Myopathies.

Background

Idiopathic inflammatory myopathies (IIM) can be subdivided in different categories: dermatomyositis (DM), immune-mediated necrotising myopathy (IMNM), antisynthetase syndrome, which is in fact an overlap syndrome, and inclusion body myositis (IBM). Previous ENMC workshops have focused on consensus on diagnosis and management of DM and IMNM. Muscle imaging plays an important role in the diagnostic process in IIM and might also be helpful for monitoring disease progression, which serves natural history studies and clinical trials. All agreed that MRI has three advantages: a) selection of a suitable site for a muscle biopsy, b) visualisation of muscle volume and c) capability to differentiate active inflammation from chronic damage. Despite these advantages, there is still no generally accepted recommendation for the performance and evaluation of the imaging methods.

Aims of the workshop

The aim of the workshop is to define recommendations concerning main technical imaging parameters and to propose a universally applicable evaluation system. In order to streamline the workshop discussions a questionnaire was distributed prior to the meeting.

Workshop deliverables

- To present the applications of MRI by discussing the results of the questionnaire.
- To provide draft recommendations on potential future imaging techniques and protocols to diagnose IIM disorders.
- To define a research agenda for the topics that are still in need of evaluation.
- To publish a separate ENMC reference paper, which helps clinicians, radiologists and patients around the globe to use the available imaging techniques in a standardised manner.

Prof Marianne de Visser said about the hybrid set-up at the 255th ENMC workshop:

"With the hybrid set-up we could bring the indispensable ideas and visions of the people online into the meeting."

She explained that 9 out of 18 invited persons were not able to travel to the Netherlands for reasons of Covid-19, pregnancy, institutes restricting travel, CO2 impact, hinderance at airports and strikes with trains.

268th ENMC International Workshop: Genetic diagnosis, clinical classification, outcome measures, and biomarkers in FSHD: relevance for clinical trials

Background

During the last few years, more than 20 companies have announced the development of a specific programme on FSHD. Fulcrum Therapeutics is the only one with an ongoing advanced stage (phase 3) clinical trial with their lead candidate drug "Losmapimod". Few other companies have announced being at the final preparation of the investigational new drug stage, and several experimental (phase 1/2) clinical trials are expected in the coming years.
This development underscores the importance of the collaboration between European experts to reach trial readiness. Therefore, FSHD Europe launched the FSHD European Trial Network (FSHD ETN), see also picture on page 19. In this 268th ENMC workshop, the first three ETN workgroups (WG1-3) came together. In the 265th ENMC workshop, the members of the 4th ETN workgroup (WG4) on MRI imaging came together, which was described previously in this impact report.

Aims of the workshop

- Strengthen the collaboration within the FSHD ETN in general, and more specifically within the three defined FSHD workgroups (see below).
- Improve the visibility of the FSHD ETN.
- Build and extend connections with pharmaceutical companies.
- Make a start with joint grant proposal(s).

Workshop discussions

The participants shared their clinical expertise and research undertaken in FSHD and lively discussions took place in the three different workgroups:

- Patient organisations and charities (FSHD Europe, FSHD Global and FSHD Society) presented their aims and main projects.
- Their experience helping companies recruit for their clinical trials and the FSHD European Patient Survey on patient expectations of future trials were presented.
- Various possibilities of collaboration between FSHD Europe, FSHD Society and FSHD global were discussed, including translation of the extensive information on the website of FSHD Society into various languages (for the FSHD Alliance Website) and reaching out to countries not yet actively involved.
- The FSHD Society will discuss with FSHD Europe and the ETN in which way they can collaborate in the organization of the FSHD International Research Conferences, and if a patient conference can take place at the same time (FSHD Connect).
- The different networks (TREAT-NMD, ETN, CTRN) aim to collaborate as on generic topics and operate regionally when necessary, all reaching towards the same aim.

Onsite and online participants of the 268th Workshop on FSHD.

269th ENMC International Workshop: Clinical trials in DMD: Ten years on, what have we learned? How can we optimize future trial design?

Background

The last ten years have seen an explosion of therapeutic innovation in Duchenne muscular dystrophy (DMD). At least a dozen new therapeutic entities have been evaluated in almost 40 potentially pivotal placebo-controlled interventional clinical trials. And yet, to date no new therapeutics have demonstrated sufficiently compelling evidence of clinical efficacy to secure full marketing approval from regulators.

Aims of the workshop

This workshop was organised to discuss participants' experiences of clinical trials in DMD over the last decade, both those that failed to meet the expected clinical endpoints and also recent successes.
The workshop did not consider aspects related to trials failed due to toxicological issues but was focused on learning from the clinical trial design, patient recruitment and execution to mitigate risks for future studies and improve clinical trial success rate for patients with DMD. A table listing all interventional clinical trials in DMD over the past decade was provided, together with the final outcome,e.g., regulatory approval, programme continuing, programme terminated.

Workshop deliverables

1. A consensus agreement on the specific statements to make in answer to the question "What have we learned?".
2. A review article: systematic review of trials in DMD of the last ten years, along with an objective assessment of what has been learned from those trials (see consensus agreement above).
3. A specific plan and action items for interacting with regulators, in order to further discuss regulatory perspectives to guide upcoming clinical trial design and analysis.

The group focused on the improved understanding of the variability in disease progression rates in DMD trials. Drug companies have sought to reduce variance by using strict inclusion and exclusion criteria to enroll patients who are in a more predictable disease phase: slowly declining but still able to walk. They discussed their experiences and hurdles in the execution of clinical trials.
An important point that was brought up relates to the fact that regulators will often require that a clinical trial must not only meet its primary endpoint but also the various secondary endpoints. While consistency between the primary and secondary endpoints strengthens evidence of a drug working, it may be that not all endpoints are as responsive to treatment. Composite endpoints were discussed as a potential solution for this, which will be investigated further.

Members of the advocacy groups and parents of boys with DMD stressed the burden of clinical trials, especially when frequent visits to the treatment centres are required. The transfer of responsibilities between the experimental therapy center and the clinical care team sometimes caused confusion.
The recommendation of the advocacy groups is to have a clear care pathway document at the inception of the clinical trial.

A strongly-voiced concern relates to the duration of placebo-controlled studies, in which DMD boys could be randomized for 12, 18 or even 24 months to receive a placebo. Moreover, there was concern over the number of muscle biopsies that are required of children in trials. Hence, there was discussion on strategies that could ensure that rapidly deteriorating children could be switched from the placebo to the active treatment arm, a strategy called a rescue protocol.

Participants of 269th Workshop on Duchenne muscular dystrophy (DMD). Mr Frank van Ieperen, who is affected by DMD, provided his input during this meeting. Frank is the chair of the Foundation "Dromen voor Duchenne" in the Netherlands, whose aim is to realise wishes of young and old patients with DMD (https://www.dromenvoorduchenne.nl/).

3.3 Participants at ENMC workshops in 2022

The ENMC strives for diversity in its workshop participants to ensure that a broad consensus can be reached at the meetings by having all relevant stakeholders around the table.
For each workshop that took place in 2022, the numbers of different stakeholders are shown in the table on the next page.

Clinicians and basic researchers formed the majority of the participants (69%), with an average of 55% clinicians and 14% basic researchers per meeting, which reflects the predominantly clinically-orientated nature of the workshops held in 2022. Connecting basic researchers with clinicians to bridge the lab and the clinic and bring the fundamental science closer to the clinic is one of the aims of the ENMC.

Through the ENMC Patient Participation Programme we aim to ensure that at least 10% of the participants of each workshop are persons affected by a neuromuscular condition, parents or advocates of these patients and/or representatives from a disease-specific patient or funding organisation. In 2022, these two groups made up 13% of total participants; the patients' voice was well represented.

On average two Early-Career researchers attended each ENMC workshop this year, showing an improvement as compared to previous years. ENMC supports the integration of the next generation of clinicians and basic scientists in established neuromuscular networks via its Early-Career Programme and Mid-Career Mentoring Programme.

In 10 workshops, where it was relevant, we also had representatives from pharmaceutical companies and regulatory agencies.

No	Workshop Title	Participants	Clinicians	Basic researchers	Translationel researchers	Patients	Patient representatives	Early-Career researchers	Industry	Regulatory	Other*
254	Formation of a European network to initiate a European data collection, along with development and sharing of treatment guidelines for adult SMA patients	35	27	2		2	1	2	1		
262	Standards of Care for the Dysferlinopathies	35	24	3	1	3	2	2			
260	Congenital Myasthenic syndromes	22	11	2	3	1	1	2	2		
258	Genetic Epidemiology and Clinical Trial Readiness in Encephalomyopathy of Leigh Syndrome	30	15	5	2	1	3	2	2		
266	Remote delivery of clinical care and validation of remote clinical outcome assessments in neuromuscular disorders: a response to Covid-19 and proactive planning for the future	31	16	4		2	4	3	2		
265	Muscle Imaging in Facioscapulohumeral Muscular Dystrophy (FSHD): relevance for clinical trials	27	14	4	2	2	1	2	2		
263	Focus on female carriers of dystrophinopathy: refining recommendations for prevention, diagnosis, surveillance and treatment	21	12	2	2		2	3			
267	Psychological Interventions for improving quality of life in slowly progressive neuromuscular disorder	27	19	2		4		2			
257	The 3rd ENMC workshop on Dystroglycan and the Dystroglycanopathies	18	6	5	2	1	1	2	1		
261	Management of safety issues arising following AAV gene therapy	32	10	5	3	1	3	2	8		
253	Skeletal muscle laminopathies - natural history and clinical trial readiness	30	15	7		2	4	1	1		
255	Muscle imaging in Idiopathic Inflammatory Myopathies	22	17	2		1		2			
268	Genetic diagnosis, clinical classification, outcome measures, and biomarkers in FSHD: relevance for clinical trials	32	15	8	1	3	2	3	1		
269	Clinical trials in DMD: Ten years on, what have we learned? How can we optimize future trial design?	24	10	2	1	1	3	2	3	1	1
Average of 14 workshops (n)		**28**	**15**	**4**	**1**	**2**	**2**	**2**	**2**	**0**	**0**
%		100%	55%	14%	4%	6%	7%	8%	6%	0%	0%
Total of 14 workshops (n)		**387**	**211**	**53**	**17**	**24**	**27**	**30**	**23**	**1**	**1**

**Other: health economics specialist*

New numbers to be proud of in 2022

Patients and patient representatives

This year we welcomed 24 patients and 27 patient representatives (parents, patient associations, patient advocates) to ENMC workshops. They all gave a presentation, asked questions and intermingled in the discussions, which was very helpful for the researchers and clinicians in the workshops to learn the patients' needs and interests.

Researchers

We managed to hold 14 workshops in 2022 catching up on workshops planned before and during the pandemic, with the attendance of 53 basic researchers, 17 translational researchers and 211 clinicians, respectively 14%, 4% and 55% of the total participants. The Early-Career Programme enabled 30 young researchers and clinicians to attend the ENMC workshops and promote their entry in the neuromuscular network.

Sponsors

In 2022, the ENMC was sponsored by nine full partners and four associated partners. The ENMC Company Forum supported our activities through the contributions of nine pharmaceutical companies. We are very thankful for the support from all these partners and acknowledge them with gratitude.

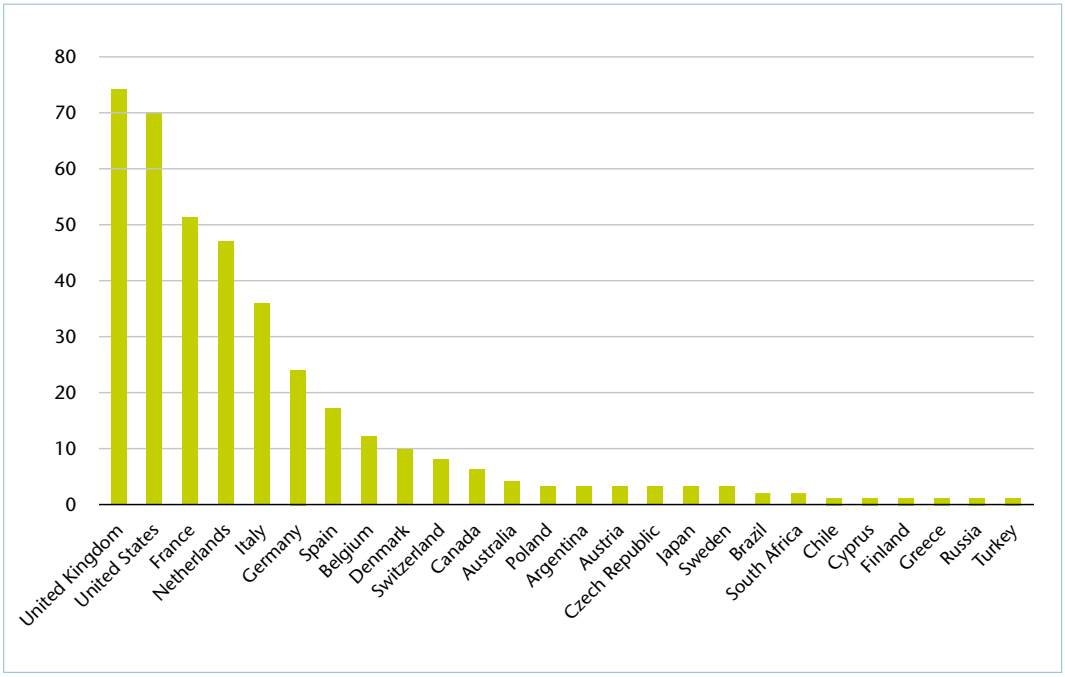
In addition to these permanent sponsors, we also would like to thank the great contributions of different organisations which co-sponsored specific workshops in 2022.

3.4 Countries represented in ENMC workshops in 2022

One of the key criteria for a workshop approval by the ENMC is the geographical balance of the participants. The ENMC is convinced that a wide coverage of countries in the workshops is important, to make sure that broad consensus is reached at ENMC workshops. This will help to start international research collaborations, ensure the standardisation of healthcare provision for people affected by a neuromuscular condition, and improve the quality of diagnosis and treatment for patients worldwide.

In 2022, many countries from all over the world were represented at the ENMC workshops (see table below), with a predominance of the ENMC full member countries (United Kingdom, France, The Netherlands, Italy, Germany, Denmark and Switzerland) and some non-member countries like USA, Spain and Belgium.
Non-European countries like Argentina, Australia, Brazil, Canada, Chile, Japan, Russia and South Africa were also well represented by individual researchers and clinicians at the 14 ENMC workshops in 2022.

Total number of participants per country in ENMC workshops 2022



4 Creating global awareness about ENMC workshops

4.1 Publication and dissemination of workshop outcomes

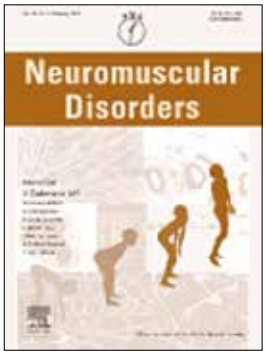
Informing patients and their families about the achievements of ENMC workshops is a key priority of the ENMC. For this purpose, a workshop lay report in English is written by workshop participants and published on the ENMC website within two weeks after the workshop. Lay reports are then translated into many different languages to increase their accessibility for people worldwide. The European partner organisations and other co-sponsors help to disseminate these translated lay reports via their local patient networks and the ENMC creates awareness on social media (Twitter name: _ENMC; LinkedIn: ENMC group) during the workshops and whenever lay reports are published on its website.

The ENMC maintains an online archive of all workshops organised since 2000, which provides access for the general public to the outcome of the workshops over the years:

https://www.enmc.org/publications/workshop-reports/

Research community

Researchers, clinicians and healthcare providers who are active in the research field of rare neuromuscular disorders need to be able to read about the scientific results of ENMC workshops in the literature. Therefore, it is mandatory that workshop organisers submit a full workshop report to the journal Neuromuscular Disorders within 6 months after the workshop. Since 2021, Early-Career Researchers who made a significant contribution to the organisation of the workshop and the writing of the lay and full report, are nominated to become co-authors on the full report.



ENMC-workshop derived publications are cited 24% more than average (100%). In bibliometric terms this means that they have a "high impact" in the NMD research field.

4.2 International conferences in 2022

ENMC representatives have attended the following international congresses:

- Cure CMD family conference, Nashville, USA (June 30-July 3 2022).
- Belgian Patient Day, Brussels, Belgium (5 July 2022).
- International Congress on Neuromuscular Diseases (ICNMD), Brussels, Belgium (5-9 July 2022).
- 3rd RyR-1 International Family Conference, Pittsburgh, USA (22-24 July 2022).
- Pre-congress symposium on: "Uniting myology forces in Europe?" prior to the Myology meeting, Nice, France (12 September 2022).
- Myology, Nice, France (12-16 September 2022).
- TREAT-NMD 7th International Conference, Vancouver, Canada (7 December 2022).

Pre-Congress-Symposium: uniting Myology forces in Europe?

Moderators : Alexandre MEJAT (Evry, France), Sabrina SACCONI (Nice, France)

- **The Italian Association of Myology - networking Italy toward connecting Europe** > Gabriele SICILIANO (Pisa, Italy)
- **The British Myology Society** > Rosaline QUINLIVAN (London, UK)
- **Euro-NMD: European Reference Network** > Carla D'ANGELO (Paris, France)
- **ENMC: Connecting people** > Alexandra BREUKEL (Baarn, The Netherlands)
- **FILNEMUS: The French neuromuscular network** > Shahram ATTARIAN (Marseille, France)

ENMC was invited as a speaker at the pre-congress symposium entitled: "Uniting myology forces in Europe?". Dr Alexandra Breukel held a presentation explaining that ENMC is an example, already for 30 years, of European integration of myology forces. Already from the beginning, ENMC opened its doors for a multidisciplinary group of workshop participants from all over the world. Within the internal organisation, the board members representing the main patient organisations that sponsor the ENMC, work closely together with the Research Committee members, thereby securing the cross-talk between the NMD patient and research communities. "Through its activities, ENMC offers a real step forward in connecting people world-wide to make progress in the treatment and care of patients with neuromuscular disorders."

5 The ENMC Mid-Career Mentoring Programme

This programme has been developed for people who seek mentoring in order to acquire skills on their way toward becoming independent researchers and/or potential future leaders in the NMD field. These individuals typically are in the stage in their careers where they are developing their own research plans and have a proven track record in the neuromuscular field. They have established research teams and collaborative networks. The guidelines and the mentee and mentor forms can be found on the ENMC website:

Mid-Career Mentoring Programme

https://www.enmc.org/mid-career-mentoring-programme/introduction/

Mentees 2021

DR AUREA MARTINS-BACH is a post-doctoral researcher at the University of Oxford (United Kingdom), where she leads the preclinical imaging research in the Physics Group at the Wellcome Centre for Integrative Neuroimaging (WIN).

Aurea's mid-career mentors are Drs A. Atema (The Netherlands), Prof. M. Rüegg (Switzerland)

DR PALOMA GONZALEZ-PEREZ is an adult neuromuscular neurologist who directs the Myopathy Clinic at Massachusetts General Hospital in Boston, United States.

Paloma's mid-career mentors are Prof. U. Schara-Schmidt (Germany), Prof. B. Smeets (The Netherlands)

DR NICOLE VOET is a rehabilitation physician and senior researcher at the Outpatient Clinic for NMD of the Radboud University Medical Centre, Nijmegen, and rehabilitation center Klimmendaal, Arnhem, The Netherlands.

Nicole's mid-career mentors are Prof. H. Lochmüller (Canada), Dr A. Urtizberea (France)

DR ROSSELLA AVAGLIANO TREZZA is a basic and translational researcher, currently a post-doc at the Maastricht University Medical Centre in The Netherlands.

Rossella's mid-career mentors are Prof. A. Aartsma-Rus (The Netherlands), Dr S. Tromp (The Netherlands)

Mentees 2022

DR LAURE GALLAY is a MD, PhD specialized in clinical immunology and rare diseases, she is currently performing a postdoctoral fellowship at the University of Geneva (Switzerland), carrying out investigations on the involvement of muscle stem cells in the pathogenesis of inflammatory myopathies.

Laure's mid-career mentors are Dr C. Wallgren-Pettersson (Finland), Dr A. Mammen (United States)

DR MERT KARAKAYA is a pediatrician, currently in the final year of his residency in Human Genetics at the Institute of Human Genetics, University of Cologne (Germany).

Mert's mid-career mentors are Prof. C. Bönnemann (United States), Prof. M. Vainzof (Brasil)

DR ERIC VOORN is working as a senior researcher at the Department of Rehabilitation Medicine of the Amsterdam University Medical Center in The Netherlands.

Eric's mid-career mentors are Prof. V. Straub (United Kingdom), Prof. A. Oldfors (Sweden)

6 Resources and financial management in 2022

Financial summary 2022

Annual accounts for the year 2022 were compiled in accordance with Guideline C1 for the reporting of small-sized non-profit organisations as published by the Dutch Accounting Standards Board.
The financial accounts are drawn up in Euros.

In the summary table below, the overall income and expenses over the year 2022 are shown in comparison with the figures for the previous financial year 2021.

Statement of income and expenses for the year 2022 in Euros (€)		
	2022	2021
INCOME		
Full Partner contributions	231.000	231.000
Associated Partner contributions	20.000	10.000
Company Forum contributions	124.940	84.204
Other contributions	57.659	5.000
Total income	**433.599**	**330.204**
EXPENSES		
Personnel expenses	163.284	183.075
Rental expenses	11.574	11.574
Activity (workshop) expenses	113.788	22.716
Organisational expenses	60.747	53.801
Total operating expenses	**349.393**	**271.166**
Operating result	84.206	59.038
Interest income	– 1.602	– 946
Net result	**82.604**	**58.092**
APPROPRIATION OF RESULTS		
Development reserve - release	– 35.407	–
Development reserve withdrawal*	– 20.195	– 20.746
Other free reserves	138.206	78.838
CASH AT BANKS ON 31 DECEMBER	**659.123**	**631.374**

**Note: Withdrawal means that these costs were made in 2022 and could be taken from this provision.*

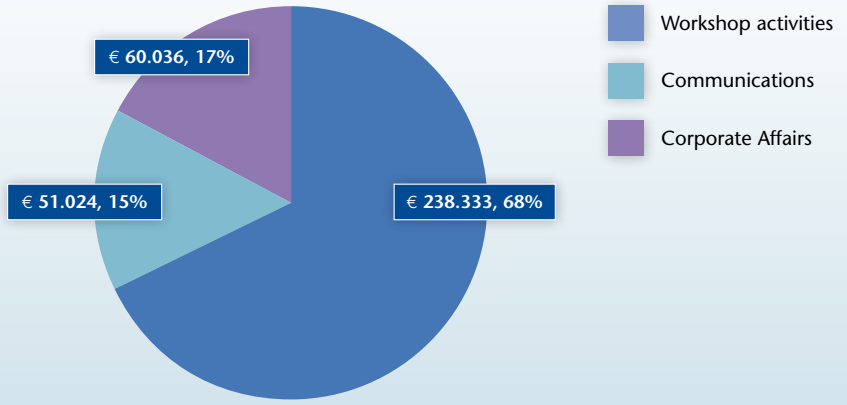
Opinion of the auditors

The independent accountants have verified and approved the annual accounts. For a full PDF version of the annual accounts report of 2022, please visit the ENMC website:

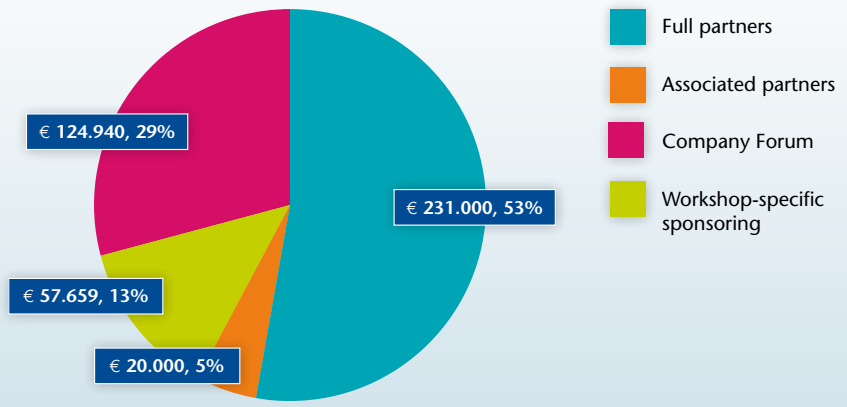
https://www.enmc.org/about-us/annual-report/

The distribution of income from the different ENMC supporters and the distribution of costs over the key accounts: workshop activities, corporate affairs and communications, are provided in the two diagrams.

Distribution of costs **2022**



Distribution of income **2022**



7 Governance in 2022

7.1 The ENMC Executive Committee

The ENMC is governed by an Executive Committee consisting of representatives of ENMC partner organisations.

Composition of the ENMC Executive Committee on 31 December 2022
Dr K. Adcock (United Kingdom)
Dr A. Ambrosini (Italy)
Dr S. van den Berge (The Netherlands)
Mr H. Ib Jørgensen (Denmark)
Dr I. Meijer (vice-Chair, The Netherlands)
Dr A. Méjat (Chair, France)
Dr A. von Moers (Germany)
Dr R. Willmann (Switzerland)

7.2 The ENMC Research Committee

The ENMC Research Committee is responsible for reviewing the scientific content and quality of the workshop applications and advises the Executive Committee on awarding the grants for ENMC workshops.

Composition of the ENMC Research Committee on 31 December 2022
Dr A. Buj-Bello (France)
Dr A. Ferreiro (Chair, France)
Prof. Dr N. Goemans (Belgium)
Prof. Dr E. Gomes (Portugal)
Prof. Dr H. Jungbluth (United Kingdom)
Prof. Dr C. Kornblum (Germany)
Dr M. Olivé (Spain)
Prof. Dr T. Sejersen (Sweden)
Dr G. Tasca (Italy)
Prof. Dr V. Timmerman (Belgium)
Dr N. Voermans (The Netherlands)

ENMC Executive Committee meeting in November 2022.

ENMC Research Committee meeting in November 2022.

7.3 The ENMC Office

The office takes care of the daily business of the ENMC.

ENMC Office staff on 31 December 2022
Dr A. Breukel (Managing Director)
Ms P. van Dongen (Programme Manager)
Ms F. Ott (Workshop Manager)
Ms A. Zittersteijn (Workshop Manager,
not on the picture),
Ms T. van Esch (Freelance Workshop Assistant)
Ms J. Schellekens (Freelance Workshop Assistant)

ENMC office staff.

8 A special thank-you to all our partners and supporters

It is thanks to the continuous support of the eight European patient organisations that the ENMC is able to facilitate and organise, on average, eight workshops per year. With support from additional partner organisations, such as condition-specific associations, associated partners and members of the ENMC Company Forum, we are also able to invite participants from non-ENMC countries and facilitate the attendance of Early-Career Researchers, patients and patient representatives.

ENMC full partners

AFM TÉLÉTHON
INNOVER POUR GUERIR

Deutsche Gesellschaft für
Muskelkranke e.V. DGM

FONDAZIONE
Telethon

fsrmm
fondation suisse de recherche sur les maladies musculaires
fondazione svizzera per la ricerca sulle malattie muscolari
schweiz. stiftung für die erforschung der muskelkrankheiten

Muscular Dystrophy UK
Fighting muscle-wasting conditions

MUSKELSVINDFONDEN

PRINSES BEATRIX SPIER FONDS
KRACHTIG TEGEN SPIERZIEKTEN

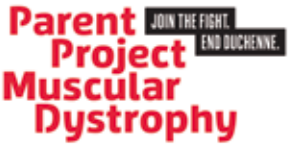
SPIERZIEKTEN NEDERLAND

ENMC associated partners

Finnish Neuromuscular Disorders Association

Members of the Company Forum

Workshop-specific sponsors in 2022



9 Looking forward to 2023 and beyond

9.1 Workshops in 2023

In 2023 we anticipate to return to full face-to-face meetings. Two ENMC workshops have already taken place and at least one workshop is planned in the second half of 2023 (see table below).

Two review rounds for workshop applications are scheduled in 2023: one in the spring (submission deadline 1 March 2023) and one in the autumn (submission deadline 1 September 2023).
The workshops that are selected at these review rounds will all be planned for 2023 or 2024.
Furthermore, 1 March 2024 will be the deadline for submitting Themed Workshop Applications.

Theme 1: Challenges of complex drugs/treatments in neuromuscular disorders.

Theme 2: Data sharing in neuromuscular disorders.

People in the NMD network are encouraged to pick up one of these two themes and apply with an ENMC Themed Workshop Application.

For more information please visit the ENMC website:

https://www.enmc.org/workshops/introduction/

Preliminary ENMC programme 2023

Workshop no. and date	Topic	Workshop leaders
Workshop no. 270 10-12 March 2023 (face-to-face)	Consensus for SMN2 genetic analysis in SMA patients?	Prof. E. Tizzano, Dr E. Bertini, Dr F.D. Tiziano
Workshop no. 271 20-22 October 2023 (face-to-face)	Third ENMC meeting on SBMA: Towards a unifying effort to fight Kennedy's Disease	Dr M. Pennuto, Dr G. Sorarù, Dr L. Greensmith, Dr P.F. Pradat
Workshop no. 272 16-18 June 2023 (face-to-face)	Inclusion Body Myositis: 10 years of progress - revision of the "ENMC 2013 diagnostic criteria for IBM" and trial readiness	Prof. C. Weihl, Prof. M. de Visser, Prof. J. Schmidt
Workshop no. 273 27-29 October 2023 (face-to-face)	Clinico-Sero-Morphological Classification of the Antisynthetase Syndrome readiness	Prof. Y. Allenbach, Prof. O. Benveniste, Dr A. Mammen, Prof. W. Stenzel
Workshop no. 274 19-21 January 2024 (face-to-face)	ENMC recommendations for optimizing bone strength in neuromuscular disorders	Dr L. Ward, Dr A. Moretti, Dr D. Weber, Dr N. Voermans
Workshop no. 275 9-11 February 2024 (face-to-face)	Seronegative MG: an update paradigm for diagnosis and management	Dr A. Evoli, Dr L. Maggi, Dr J. Palace, Prof. J. Verschuuren
Workshop no. 276 15-17 March 2024 (face-to-face)	ENMC recommendations on optimal diagnostic pathway and management strategy for patients with exertional rhabdomyolysis worldwide	Prof. P. Laforêt, Prof. J. Vissing, Dr N. Voermans, Dr S. Bhai

9.2 International conferences in 2023

ENMC ambassadors will attend the following international congresses with a booth:

- Congress of the Medical Scientific Advisory Board of the German Muscular Dystrophy Society (DGM) e.V., Essen, Germany (24 March 2023).
- German Patient Day of the DGM, Essen, Germany (25 March 2023).
- UK Neuromuscular Translational Research Conference, London, UK (29-30 March 2023).
- Peripheral Nerve Society Annual Meeting (PNS), Copenhagen, Denmark (17-20 June 2023).
- European Pediatric Neurology Society Congress, Prague, Czech Republic (20-24 June 2023).
- International Congress on Neuropathology, Berlin, Germany (13-16 September 2023).
- Dutch Patient Day (SN), Veldhoven, The Netherlands (16 September 2023).
- World Muscle Society Congress, Charleston, USA (3-7 October 2023).

9.3 Budget for 2023

This table presents the budget forecast for 2023 as of 31 December 2022.

Budget 2023 in Euros (€)	Actuals 2022	Budget 2023
INCOME		
Full Partner contributions	231.000	231.000
Associated Partner contributions	20.000	20.000
Company Forum contributions	124.940	145.000
Other contributions	57.659	20.000
Total income	**433.599**	**416.000**
EXPENSES		
Personnel expenses	163.284	241.000
Rental expenses	11.574	12.500
Activity expenses	113.788	140.000
Organisational expenses	60.747	60.000
Total operating expenses	**349.393**	**453.500**
Operational result	84.206	– 37.500
Interest income	– 1.602	– 700
NET RESULT	**82.604**	**– 38.200**

Colophon

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