



ENMC Impact Report 2018

Our year in highlights

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1 Message from the Chair of the Executive Committee

2018 was a special and productive year for the ENMC. A year in which we have funded twelve workshops, the highest number ever. This shows that the experts in the neuromuscular field are more than ever using ENMC workshops to make the necessary progress in the development of treatments and good care. The fact that the ENMC concept is successful, is also apparent from the impact analysis that was done this year. We are proud that the ENMC received the “high impact label”.

Other special activities in 2018 focused on the 25th anniversary of the ENMC. One that I would like to mention in particular is the workshop on “the position of the neuromuscular patient in Shared-Decision-Making”. A special workshop with different stakeholders who shared their vision on the importance of patients’ involvement in neuromuscular research and care management.

What is most characteristic of the ENMC for me is that we do it together. The involvement and devotion of many is needed to move forward. Within the neuromuscular field, this is the key to success. My special thanks go to all those directly involved in the ENMC; patient organisations, patients, members of the Research and Executive Committee, research-



Dr Ellen Sterrenburg, Chair of the Executive Committee

ers, clinicians, members of our Company Forum and the ENMC team in Baarn. Together we reach more and we work hard to ensure that people with a neuromuscular disease have access to the best possible care and eventually also cure.

*Dr Ellen Sterrenburg,
Chair of the Executive Committee*

2 The mission of the ENMC

More than 25 years ago, a group of scientists and clinicians, together with parents of children affected by a neuromuscular condition, started the European Neuromuscular Centre (ENMC). They had in mind the ultimate goal to improve diagnosis, accelerate the search for effective treatments and improve the quality of life of people with a neuromuscular condition. To achieve this goal, it was and still is of utmost

importance that experts in this field of (ultra) rare disorders share their knowledge and experience and collaborate in research worldwide. The ENMC encourages and facilitates this collaborative aim through the organisation of small interactive workshops for multidisciplinary groups of researchers, clinicians and persons affected by a neuromuscular condition – a unique concept in the scientific community.

ENMC Mission Statement

The mission of the 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 optimizing standards of care to improve the quality of life of people affected by neuromuscular disorders.



“Connecting people”

3 The ENMC workshops in 2018

In 2018, a record high number of 22 workshop applications was submitted to the ENMC. Of these 22 applications, 12 were granted an award for an ENMC workshop to take place in 2018 and 2019 (nine were originally budgeted for, but extra funding was allocated to approve three more). The high number of workshops approved in 2018 (55%), indicates the high quality of the submitted applications.

3.1 Summary of ENMC workshops held in 2018

In 2018, six workshops were organised, of which five took place in the vicinity of Amsterdam and one in Milan. The workshops are listed in the table below.

ENMC workshops in 2018

Workshop no./Date	Topic	Workshop leaders
Workshop no. 235 19–20 January 2018	Special Anniversary Workshop: “The position of the neuromuscular patient in Shared-Decision-Making”.	Prof. H. Lochmüller and Prof. A. Tibben in collaboration with the ENMC board
Workshop no. 236 1–3 June 2018	Bone protective therapy in Duchenne Muscular Dystrophy: Determining the feasibility and standards of clinical trials.	Prof. V. Straub, Dr J. Wong, Prof. L. Ward and Dr R. Quinlivan
Workshop no. 237 14–16 September 2018	GNE myopathy (also known as HIBM, Nonaka disease, and quadriceps sparing myopathy) (GNEM).	Prof. H. Lochmüller, Dr J. A. Urtizberea, Prof. Z. Argov and Prof. I. Nishino
Workshop no. 238 30 November– 2 December 2018	Updating management recommendations of cardiac dystrophinopathy.	Dr J. Bourke, Prof. D. Duboc, Dr M. Guglieri and Dr T. Evangelista
Workshop no. 245 7 December 2018	One-Day meeting: Preparation of common recommendations on muscle pathology laboratory methods by the EURO-NMD Pathology Workgroup.	Prof. B. Udd, Prof. W. Stenzel, Prof. A. Oldfors
Workshop no. 239 14–16 December 2018	Clinicopathological Classification of Dermatomyositis.	Prof. A. Mammen, Dr Y. Allenbach, Prof. W. Stenzel



Participants of the 235th ENMC workshop on “The position of the neuromuscular patient in Shared Decision Making”, which took place at the ATA hotel, Expo Fiera in Milan, Italy.

235th ENMC international workshop: “The position of the neuromuscular patient in shared decision making”

This workshop was organised to celebrate the 25th Anniversary of the ENMC. For this special occasion, it was held in Milan and was attended by 45 participants from 15 different countries. The group represented a wide range of experts: patients and parents, representatives from neuromuscular disease organisations, clinicians, healthcare professionals, researchers, societal and policy researchers, psychologists, ethicists, and representatives from regulatory authorities and pharmaceutical companies.

In the field of neuromuscular disorders, the engagement of patients has long been recognised as key issue, and the ENMC has sought to encourage patient participation in its workshops. With this anniversary workshop, the ENMC aimed to further strengthen patient participation for a set of important topics related to neuromuscular research and care management:

- 1 psycho-social support of families going through the processes of screening and diagnosis
- 2 transition from child to adolescent to adult patient
- 3 research into areas that have a major impact on daily life (nutrition, pain, fatigue)
- 4 registries and biobanks
- 5 clinical trial design
- 6 regulatory and consenting processes

The aims and outcome of the workshop were:

- **to create a white paper** that positions the patients in neuromuscular disorders as co-creator and co-responsible partner. This document can be used in discussions with local, regional, national and international stakeholders, as well as with fellow patient organisations to achieve endorsement and support for change. The white paper will be finished in 2019.
- **to improve awareness** by disseminating and presenting to professionals working in the field of neuromuscular disorders the outcomes of this workshop and the white paper. The ENMC will publish two full workshop reports^{1, 2} in relevant scientific journals, and will translate a lay report into several languages.

¹ Lochmüller *et al.* The Position of Neuromuscular Patients in Shared Decision Making. Report from the 235th ENMC Workshop: Milan, Italy, January 19–20, 2018. *Journal of Neuromuscular Diseases* 6 (2019) 161–172.

² Ambrosini *et al.* “Be an ambassador for change that you would like to see”: a call to action to all stakeholders for co-creation in healthcare and medical research to improve quality of life of people with a neuromuscular disease. Second report from the 235th ENMC workshop in Milan. Accepted for publication in the *Orphanet Journal of Rare Diseases* (2019).

Dr Valeria Sansone, Director of the NEMO Clinical Centre, Milan, Italy:

“I am currently writing a grant application and after this workshop, I will change it by including patient representatives and/or advocacy groups participation throughout the whole design of the trial.”

Here, the role of patient organisations and clinical centres will be key to set the stage for change and transformation in patient relations with all stake-

holders (researchers, regulatory agencies and industry).

236th ENMC international workshop: “Bone protective therapy in Duchenne muscular dystrophy”

Muscle strength and bone strength are closely related. In Duchenne muscular dystrophy (DMD), muscle weakness, corticosteroid treatment and delayed puberty lead to an increased risk of bone fractures (limb and vertebral). Fractures have serious consequences, including pain, loss of ambulation, and fat embolus syndrome.

Bone protective therapy involves detection and prevention of fractures and treatment of fractures to reduce pain. Most boys with DMD have delayed puberty; management of this is important for bone health. As an example, bisphosphonates form a class of drugs that prevents the loss of bone density. During the workshop it was concluded that oral bisphosphonates are not as effective as intravenously administered bisphosphonates. Furthermore,

compliance with oral treatment is poor. Intravenous bisphosphonates reduce pain and promote vertebral fracture healing, but there is a risk of important side effects, usually with the first dose. Newer bone protective drugs are increasingly becoming available and could be studied in relation to DMD.

In conclusion, clinician and patient education on bone health is essential to advance the field of bone health in DMD. A small placebo-controlled trial for prevention of first fractures is necessary, together with trials comparing bisphosphonates with new treatments to treat fractures and ultimately to optimise the care of patients with DMD. Future steps include dissemination of knowledge across all stakeholders, establishing a working group and exploring funding possibilities.

Workshop organisers and patient representatives at the 236th ENMC workshop on “bone protective therapy in Duchenne muscular dystrophy”, which took place at the Courtyard Marriott hotel, Hoofddorp, The Netherlands.

From left to right: Mr Frank van Ieperen, Dr Ros Quinlivan, Prof. Leanne Ward, Dr Jarod Wong, Prof. Volker Straub, Ms Pat Furlong and Mrs Angela Stringer.





Participants of the 237th ENMC Workshop on “GNE myopathy”, which took place in the Courtyard Marriott Hotel, Hoofddorp, The Netherlands.

237th ENMC international workshop: “GNE myopathy”

GNE myopathy is an inherited rare muscle-wasting disorder caused by mutations in the GNE gene (where GNE is an abbreviation for the mutated gene UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase). The GNE gene contains the instructions to make an enzyme that has a key role in the production of sialic acid in the body, which is important for muscle strength. A deficiency of this enzyme in the muscle cells leads to increasing disability. GNE myopathy is identified in many research laboratories worldwide. There is currently no approved treatment or medication available that would cure the disease or slow down the disease progression.

The workshop participants reviewed the current medical and scientific knowledge relevant to GNE myopathy to achieve a better understanding of GNE myopathy epidemiology, phenotype and genetics. They agreed on a standard of care for GNE myopathy patients, discussed the strength and weakness of the currently available animal models, and attempted to improve their understanding of the biochemical consequences of the GNE defect on muscle tissue leading to muscle damage and weakness. Building on the latter topic, participants deliberated on other potential treatments for the condition, such as gene therapy and stem cell therapy.

The follow-up actions agreed upon at the meeting were:

- to develop patient-friendly inclusive information
- to collect standardised clinical information for further research in accessible formats, to help build a robust cohort
- to work collaboratively towards treatments for patients
- to share data and biomaterials
- to make genetic information on rare GNE gene variants available for genetic diagnosis
- to propose standards of care for GNE myopathy patients.

The group concluded that further (pre)clinical research is required to develop suitable models of the disease in laboratory animals, to identify molecules in patients’ blood and muscle to monitor disease progression and response to treatment (biomarkers), and to validate clinical endpoints, outcome measures and study designs for future clinical trials.

Please also read the interview with Ms Mireille Hek on page 15 of this impact report, providing the patient perspective on this important workshop.

238th ENMC international workshop: “Updating management recommendations of cardiac dystrophinopathy”

This workshop brought together neuromuscular and cardiology experts from Europe and the United States to discuss cardiac care of patients with Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD). The aim was to build on the extensive *International DMD Care Considerations 2010* and 2018 guidelines, adding the latest evidence and collating expert opinion on cardiac management of patients with conditions caused by mutations in the dystrophin gene.

Implementation of multidisciplinary care, including steroid therapy and timely support for respiratory muscle weakness, already improved survival rates in DMD. However, it is increasingly apparent that control of heart-function deterioration is critical to long-term survival. Silently progressive cardiomyopathy (loss of the heart pump function) affects almost all patients with DMD, but causes symptoms only in later years with the onset of heart failure. Currently, there is a lack of agreement about when it is most advisable for a patient to begin heart-specific medications, based on their age or test results.

Some clinicians use an ultrasound test (echocardiography) to detect any weakness in the heart’s main pumping chamber (left ventricular dysfunction), while others test for the presence of scars in the heart muscle (myocardial fibrosis) using cardiac magnetic resonance imaging (cMRI). However, the workshop concluded that, in DMD, the heart is affected from birth. As such, each testing method used to justify starting heart treatments simply reflects what each is capable of ‘seeing’ in the progressive process of heart involvement in DMD. The lack of sensitivity of standard echocardiography in detecting early abnormalities of heart muscle, and technical issues around obtaining high-quality and standardised cMRI across centres and in younger patients was recognised. The expert consensus was that families should be made aware, at around the time of

diagnosis, that heart care will be important throughout life. The particular heart drugs recommended, whether available now or to be developed in the future, and the optimum time to introduce them, depend on what they are designed to do and the balance between their effectiveness and side effects. Furthermore, specific exercise programs for patients with DMD and their positive effect on cardiovascular functioning were discussed. This topic will be central in ongoing research.

In conclusion, it was agreed that longitudinal data needs to be collected on the effects of different medications and other interventions, and that reaching agreement with regulators about clinically meaningful research outcome measures for the heart in DMD is a priority.



Workshop organisers, young scientist and patient representatives at the 238th ENMC workshop on “Updating management recommendations of cardiac dystrophinopathy”. From left to right: Prof. Denis Duboc, Dr Elizabeth Vroom, Dr Michela Guglieri, Dr Maruška Šedivá (young scientist), Dr Nick Bennet and Dr John Bourke.



Prof. Werner Stenzel talking at the 239th ENMC workshop about the mandatory testing of myositis specific auto-antibodies (MSA), such as TIF-1, Mi-2, NXP2, MDAS and SAE.

The 239th ENMC international workshop: “Clinicopathological Classification of Dermatomyositis”

This workshop brought together experts in the field of muscle inflammation (myositis) from Europe, Japan, China, Canada and the USA. Neurologists, rheumatologists, dermatologists, neuropathologists and myopathologists discussed and renewed the diagnostic criteria of dermatomyositis (DM) based on recent advances in the field. All experts agreed on the importance of mandatory testing of myositis specific auto-antibodies (MSA) in the diagnostic examination of DM patients. Auto-antibodies are antibodies attacking a person’s own normal cells. The group of experts emphasised the importance of detecting auto-antibodies to define certain subtypes of DM, which may have a characteristic clinical, pathological and even histological appearance. If the clinical presentation of a patient is classical – that is, consisting of characteristic DM-associated skin changes (e.g. DM-like rash), muscle weakness and detection of any MSA – then the diagnosis of DM may be made, even without a muscle biopsy. Moreover, the finding of characteristic skin changes, clinically observable and in a skin biopsy, in combination with MSA but without muscle functioning being affected, is also compatible with the diagnosis of DM. A more detailed definition of DM-like skin changes and histological criteria seen in the skin biopsy of an

affected skin area in a DM patient will soon be published by an international expert team of dermatologists. It was clear to all experts that the muscle biopsy was, and still is, a very valuable tool and the gold standard in the diagnostic routine. Novel, specialised immunohistochemical stains further increase the certainty of a correct histological diagnosis.

Additionally, the classification of the Anti-synthetase syndrome (ASS) was a matter of debate at this workshop. Anti-synthetase syndrome is a chronic autoimmune condition that affects the muscles and various other parts of the body. The exact underlying cause is unknown; however, the production of auto-antibodies that attack certain enzymes in the body called ‘aminoacyl-tRNA synthetases’ appears to be linked to the cause of the syndrome. These auto-antibodies against aminoacyl-tRNA synthetases can be detected with immunohistochemical staining. Recent scientific data presented at the ENMC workshop clearly highlighted the differences between DM and ASS. All experts agreed on ASS being a distinct subtype, pathophysiologically clearly different from DM. Nevertheless, ASS can, in very rare cases, be considered as DM-related.

245th ENMC International one-day meeting of the EURO-NMD Pathology Workgroup: “Preparation of common recommendations on muscle pathology laboratory methods”

All neuromuscular diseases are defined as rare diseases, and many of them are very difficult to diagnose and treat. EURO-NMD is a newly established network of European reference centres (ERNs) that provides access to expert consultations on diagnostics and care for patients with undetermined neuromuscular diseases. The pathology working group of the EURO-NMD initiative – comprising five expert members, one patient representative, and four additional muscle pathology experts, from Germany, the UK, France, Finland, Sweden, Italy, Spain, Belgium and the Netherlands – took part in a one-day meeting in Amsterdam on December 7th 2018, hosted by the ENMC. The purpose of the meeting was to finalise a EURO-NMD document on ‘Recommended Standards’ for muscle biopsy techniques to be applied in all pathology laboratories of the 61 EURO-NMD reference centres.

A survey of current practices in all ERNs was carried out in 2017 and, based on the responses, a need to standardise muscle pathology methods in Europe was evident. The pathology working group prepared a draft for such ‘Recommended Standards’ in September 2018 and the feedback from participating centers on the circulated draft was analysed and discussed. The meeting resulted in a final version on the: ‘Recommended Standards for muscle pathology’, which will be published as a meeting report in *Neuromuscular Disorders*.



EURO-NMD Pathology Workgroup participants of the 245th ENMC International Workshop, which took place in the World Trade Centre at Schiphol in Amsterdam, The Netherlands. From left to right: Prof. Benno Küsters, Dr. Teresina Evangelista, Prof. Werner Stenzel, Prof. Bjarne Udd, Prof. Martin Lammens, Prof. Caroline Sewry, Prof. Anders Oldfors and Dr. Norma Romero.

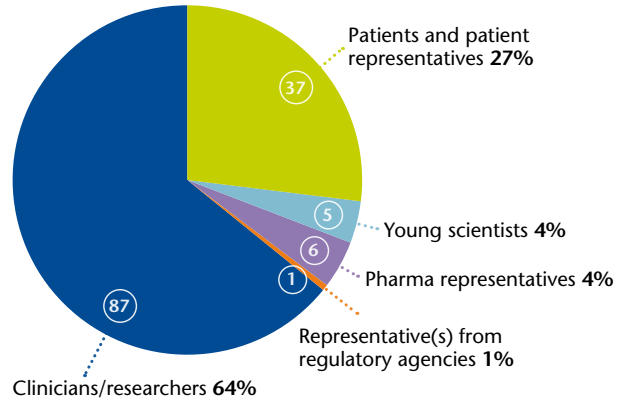
3.2 Participants at ENMC workshops in 2018

The ENMC strives for diversity in its workshop participants, to ensure that consensus can be reached at the meetings by having all relevant decision-makers around the table.

In 2018, clinicians and basic researchers formed the majority (n=87, 64%) of all 136 workshop participants. Almost 40 patients and patient representatives attended the ENMC workshops resulting in a high level of patient participation (27%) this year (in green). This was merely owing to the patient-oriented workshop in Milan; 6 patients and 16 patient representatives attended this workshop (50% of the total group of 45 participants).

The ENMC aims to invite at least one or two young scientists per workshop, and this was achieved for four of the six workshops in 2018. Representatives

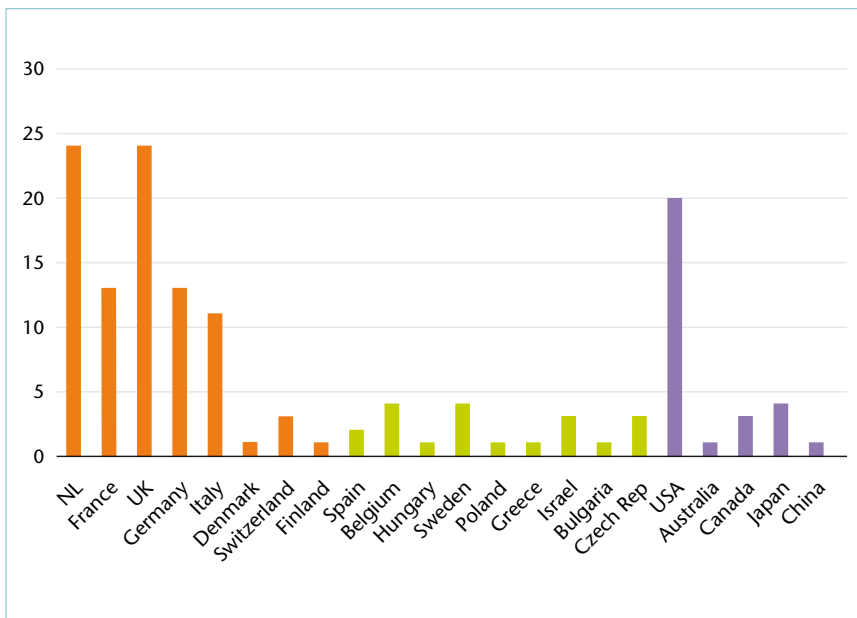
Number of representatives in ENMC workshops in 2018



from regulatory agencies, such as the European Medicine Agency, and from pharmaceutical companies were also present at the ENMC workshops last year.

3.3 Countries represented in ENMC workshops in 2018

Total number of participants per country attending workshops in 2018



The orange bars represent the eight country members of the ENMC. The green bars represent countries located in or close to Europe, but which are not a member of the ENMC. The purple bars are participants coming from continents other than Europe; these countries are not members of the ENMC.

One of the key criteria for workshop approval by the ENMC is the geographical balance of the participants. The ENMC considers a wide coverage of countries in the workshops important, to make sure that consensus reached at ENMC workshops on diagnostic and/or therapeutic guidelines can be implemented across Europe and beyond. This will help in the standardisation of healthcare provision for people affected by a neuromuscular condition, which in the end may guarantee the best quality diagnosis and treatment of patients worldwide. Many countries from all over the world were represented at the ENMC workshops in 2018; with a

large contribution from ENMC member countries (Netherlands, France, UK, Germany, Italy, Denmark, Switzerland and Finland); these countries are represented by the purple bars in the figure on page 14. Non-ENMC countries were also represented at the workshops in 2018; these are indicated by the green and blue bars. Since 2017, the ENMC has encouraged participation from Eastern European countries with a special travel grant, and this is reflected in the high level of attendance (n=6) in 2018 of clinicians/researchers coming from Poland, Hungary, Bulgaria and the Czech Republic.

3.4 The ENMC from the perspective of a patient, Ms Mireille Hek

In September 2018, the ENMC held an international workshop dedicated to GNE myopathy, which was summarised on page 10 of this impact report. In the Netherlands, to date, fewer than ten people are known to have this disorder. Ms Mireille Hek is one of them. Mireille is very active within the Dutch Neuromuscular Diseases Patient Association. She is eagerly trying to connect with others affected by this ultra-rare condition, especially in The Netherlands. Mireille was also one of the participants of the ENMC GNE myopathy workshop.

Together with two other people affected by GNE myopathy – one person from Israel and one person from the UK – Mireille represented the patients' voice

in this workshop. They worked closely together with researchers and clinicians over the weekend towards a better understanding of the underlying mechanisms, and they helped prioritise the international agenda of GNE myopathy research.

It is clear that much has been tried, in mouse models and in the clinic, but that so far nothing has led to a useful and effective treatment for GNE myopathy patients. Mireille realised that the treatment will not be available in time to cure current patients diagnosed with GNEM, but she is positive that the next generation of GNE myopathy patients will benefit from new interventions available within 10 years.



Ms Mireille Hek:

“By attending this meeting I know now what is happening in the research field: Many efforts have been made to find a treatment for this disease. However, unfortunately there is still no solution available.”



In the back from left to right: Dr Antoni Urtizbera (France), Dr Anke Willems (The Netherlands), Dr Oksana Pogoryelova (United Kingdom), Prof. Hans Lochmüller (Germany/ Canada), Prof. Ichizo Nishino (Japan), Dr Maya Davidovich (Israel), Prof. Zohar Argov (Israel). In the front from left to right: Ms Mireille Hek (The Netherlands) and Ms Mona Patel (United Kingdom).

“The importance of this workshop is that clinicians and basic researchers shared their knowledge, discussed possible solutions attacking GNE myopathy, and were very much willing to collaborate in this quest.”

One of the questions the patients raised was why GNE myopathy patients do not experience loss in muscle mass. Professor Bjarne Udd explained that there is muscle loss detected in GNE myopathy patient biopsies, however non-functional fat cells compensate for this loss in GNE myopathy, something typical for GNE myopathy. The patients were asked what their needs were, how tools (such as the wheelchair) are being reimbursed in different countries, and what they think should be prioritised on the research agenda. One of the topics the patients addressed was complications in pregnancy and the safest way to deliver. A lively discussion started about cultural differences, and there was no clear answer to the question of whether caesarean section or natural delivery is the preferred method of delivery for GNE myopathy patients. The researchers

decided to include a survey for all women affected by GNE myopathy in the new trials, to capture data on this specific topic. For Mireille, this was a nice example of patient involvement:

- 1 identifying gap(s) in knowledge among healthcare professionals by asking plain questions, and
- 2 just asking the patients for their needs, thereby helping the professionals achieve the knowledge required to solve problems clearly.

Mireille’s action steps, resulting from this workshop, are to inform GNE myopathy patients in the Netherlands about the European GNE myopathy registry (www.gnem-dmp.com) and the upcoming trials, and encourage them to actively take part in these important research initiatives.

“It really felt that all participants were equal in the workshop, whether they were patient, caregiver, clinician or researcher. I experienced the group as a strong unity, which is key to being successful in finding solutions for this devastating disease!”

3.5 Impressions of workshop participants

During the workshop weekends, we collect impressions and feedback from participants. The “dinner booklet” is filled with many breath-taking quotes, inspiring compliments and useful learning points for

future ENMC workshops. This is what keeps us going every day!

Here are some impressions of a part of the amazing people we met at the workshops in 2018:

“It’s a big pleasure for me to be a participant of the ENMC meeting. It’s proof that we have a lot of work to do, to improve the quality of life of patients with a neuromuscular disorder, and we can achieve the success only when we are strongly connected and cooperate together.”



Michal Rataj from Poland, affected by Limb Girdle muscular dystrophy, board member of EAMDA (European alliance of Neuromuscular dystrophy associations) and very active for the EPF (European Patient Federation). Michal attended the 235th ENMC workshop on shared decision-making in Milan.



“My first meeting as a young scientist in the ENMC ‘family’ and it was wonderful! I learned so much and got to know the leading people in the field of myositis.”

Dr Josefine Radke, working as neurologist at the Institut für Neuropathologie, Charité, Universitätsmedizin in Berlin. Josephine applied for the ENMC young scientist award and was selected to join the 239th ENMC workshop on myositis. ENMC paid her travel and other accommodation costs with this special grant.

4 The impact of 25 years of ENMC workshops

4.1 Publication and dissemination of workshop outcomes

The workshop results are being reported and disseminated to the patient and scientific community, respectively.

Patients and families

Informing patients and their families about the achievements of ENMC workshops is one of the key priorities of the ENMC. This is done by the workshop lay report, which is written by workshop participants and published on the ENMC website within two weeks of the workshop. Nowadays, all lay reports are translated into many different languages other than English, which increases the accessibility of these reports for people worldwide. The nine European patient member 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 whenever lay reports are published on their website.



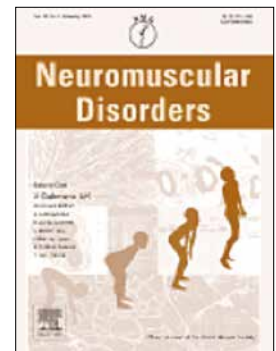
The ENMC maintains an online archive of all workshops organised since 2000, which provides access for the general public to the lay reports produced after each ENMC workshop.

See:

<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 *Neuromuscular Disorders* within 6 months of the workshop having taken place.



4.2 Bibliometric analysis of 25 years ENMC workshops in 2018

Since the foundation of the ENMC in 1992, 240 workshops have taken place, and the ENMC wanted to assess what impact these workshops have had on the neuromuscular community. The results of a qualitative impact analysis were included in the ENMC annual report of 2017. Here, we will focus specifically on the outcome of the literature analysis carried out in 2018 in collaboration with the Centre

for Science and Technology Studies (CWTS), an interdisciplinary research institute at Leiden University in The Netherlands³. The combination of data is published in *Neuromuscular Disorders*⁴.

Publication rate of full ENMC workshop reports

Since 1993, on average, 79% of the workshops have been published as full reports in *Neuromuscular*

Disorders. Since 2010, when more strict reporting guidelines were introduced, this percentage has increased to 90%.

Absolute citation scores of full ENMC workshop reports

The majority of workshop reports (87%) have been cited between 0 and 50 times, while 13% have been cited more than 50 times. The four workshop reports with the highest citation scores are:

Workshop no.	Title	Citation score
Workshop no. 124	“Gold standard for Duchenne Muscular Dystrophy therapy”	129 citations
Workshop no. 30–31	“Limb Girdle Muscular Dystrophy nomenclature”	156 citations
Workshop no. 107	“Cardiac involvement in NMD”	212 citations
Workshop no. 119	“Trial design in Idiopathic Inflammatory Myopathy”	390 citations

This evaluation is limited in that these citation scores are absolute values and therefore not corrected for differences in publication age (i.e. how many years a paper is available for citations) and cultural citation behavior per scientific area. Therefore, they cannot be compared with citation scores of other papers. In addition, the output of ENMC workshops is reflected not only by the mandatory ENMC workshop reports, but also by the spontaneous publications reflecting and/or referring to (collaborative) work initiated at an ENMC workshop.

To bypass these limitations, a literature search on ENMC workshop-derived papers was performed within the CWTS in-house Citation Index (CI) database. On the resulting list of papers, relative citation scores were identified by using Web of Science (WoS) cluster normalisation to correct for year and field differences (see next section).

Normalised citation scores of ENMC workshop-derived publications

The initial data selection yielded a validated dataset of 98 papers, of which approximately 30% were ENMC workshop reports and 70% indirect publications. Since the impact of the ENMC workshops entails not only the full workshop reports, but also follow-up research and collaboration activities after the workshop, citations scores of all 98 papers were measured. This analysis therefore reflects performance of the ENMC network, not of the ENMC as a “sole institute”. This set of papers is referred to as “ENMC workshop-derived publications”.

The output of papers started to increase around 2010, when full report publications became mandatory. The total number of citations is 1955 and yielded a mean normalised citation score (MNCS) of 1.24. This number means that the impact of this selection of 98 publications is 24% higher than the impact of the average performing paper in this literature cluster. The threshold at which CWTS assigns the ‘high impact’ label is an MNCS of 1.20; exceeding the 20% world average. ENMC workshop-derived publications were therefore assigned a ‘high impact’ label.

³ Centre for Science and Technology Studies. (2018). Bibliometric research performance of the European Neuromuscular Centre (ENMC) 2000 – 2016/17. Retrieved from: https://www.enmc.org/wp-content/uploads/2019/04/ENMC_2000-2016-Final-Report-by-CWTS-Oct2018.pdf

⁴ Breukel *et al.* The impact of European Neuromuscular Centre (ENMC) workshops on the neuromuscular field; 25 years on. *Neuromuscular Disorders*, vol. 29, (2019) 330–340.

Another important impact indicator is the PPTop10%, which gives an indication of the visibility of papers in the literature field. It identifies the proportion of the publications of a research institute that belongs to the top 10% mostly frequently cited publications in their field and publication year. A value of 20% for the PPTop10%, for instance, means that an institute has twice as many top 10% publications as expected, meaning that it was 10% more visible in the literature than expected. The PPTop10% of the 98 ENMC workshop-derived papers was 16%, which means that they had a 6% higher visibility than expected.

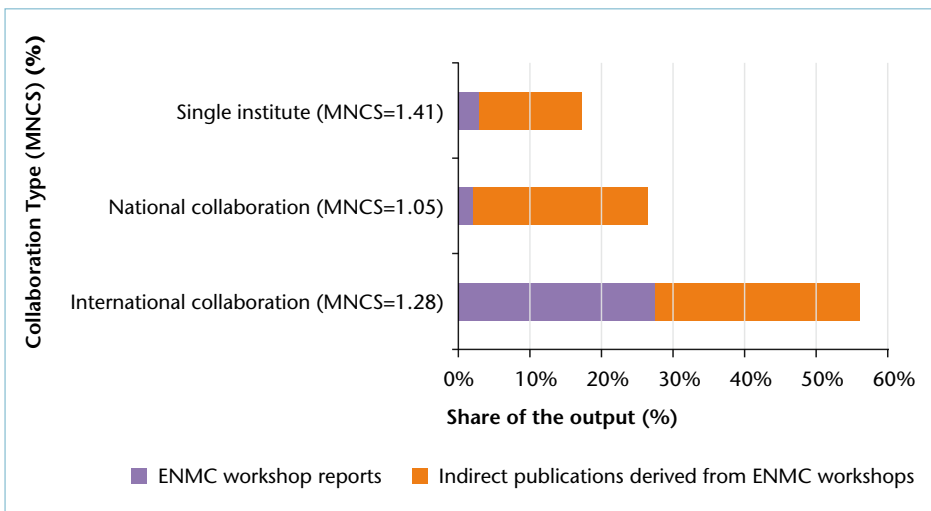
papers published by individual researchers/institutes ('single institute'), by research groups in one single country ('national collaboration'), and by research institutes across international borders ('international collaboration') (see Figure below). Publications authored by single institutes achieved the highest impact, with an MNCS of 1.41, followed by publications authored by international collaborations, with an MNCS of 1.28. These results place both in the range of 'high impact'. Publications authored by national collaborations were cited at world average (MNCS=1.05).

Collaboration Profile

As the ENMC aims to encourage and facilitate communication and collaboration in the field of neuromuscular research, CWTS performed a collaboration analysis to check for the effectiveness of the ENMC in achieving this part of its mission. In the collaboration analysis, a distinction is made between

At 57%, the share of the output is highest for those publications authored by international collaborations. This achievement reflects that the ENMC stimulates communication and international collaboration between experts in the field of neuromuscular diseases, resulting in joint scientific publications.

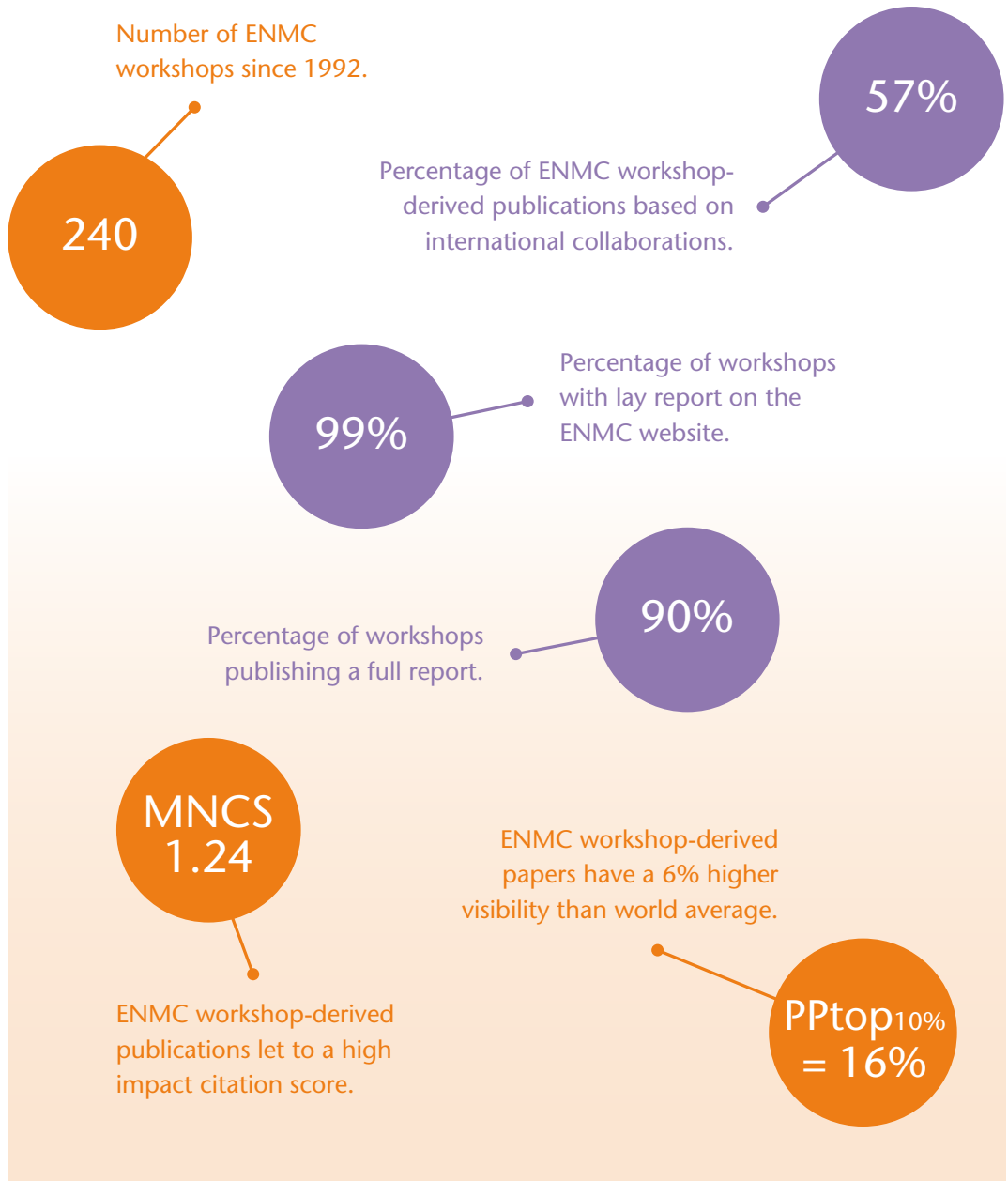
Collaboration profile for the ENMC workshop-derived publications



Collaboration profile for the ENMC workshop-derived publications (2000–2016). In this figure, the share of the output, in % of the total number of publications within the period 2000–2016 fulfilling ENMC search criteria, is drawn on the X-axis. The type of collaboration is drawn on the Y-axis, with the impact (MNCS) of each group in brackets. The ENMC workshop reports are illustrated in purple bars, the indirect publications derived from ENMC workshops in orange.

In conclusion, the citation scores and the impact of workshop-derived publications show the high degree of collaboration mediated by the workshops and the quality of this collaboration. The high output of

publications derived from a workshop (the obligatory report and follow-up publications) represents an added value for researchers and clinicians in being part of the ENMC network.



5 ENMC at international neuromuscular conferences in 2018

To meet scientists and clinicians and create awareness about the ENMC, several international conferences are being attended by ENMC every year. In July 2018, the International Congress on Neuromuscular Diseases (ICNMD) was held in Vienna, Austria and was visited by more than 1,500 researchers and clinicians working in the NMD field. In addition, members of the Research Committee and the Executive Committee represented the ENMC as ambassadors at this important meeting. The ENMC booth was clearly visible, and many young scientists and potential future workshop organisers visited us to discuss application procedures and to share their

ideas for an ENMC workshop. Many people unknown to ENMC gave written consent to enter their personal data in our database with the aim to keep them informed on ENMC activities via the bi-annual newsletters and to be able to invite them for future workshops.

The ENMC organised a special symposium at the ICNMD on 8 July 2018, to present the impact of 25 years ENMC workshops by several workshop organisers and Executive Committee members (see below the programme).

Programme

Speakers

Introduction about the ENMC

Dr Ellen Sterrenburg (Chair of the ENMC Executive Committee, Manager Policy and Research at Prinses Beatrix Spierfonds, The Netherlands)

Why opt for an ENMC workshop?

Chaired by: **Prof. George Padberg** (Research Director ENMC) and **Prof. Baziël van Engelen** (Head Neuromuscular Disorders, Radboud UMC Nijmegen, The Netherlands)

The impact of 25 years of ENMC workshops

Dr Raffaella Willmann (ENMC Executive Committee, representative of the Swiss Foundation for Research on Muscle Disease, Switzerland)

Charcot-Marie-Tooth disease at ENMC workshops

Prof. Mary Reilly (Head of Division of Clinical Neurology, MRC Centre for Neuromuscular Diseases, London, UK)

Translational Research workshop

Prof. Kanneboyina Nagaraju (Founding Chair, Department of Pharmaceutical sciences, SUNY-Binghamton University, New York, USA)

Management of ventilation problems in patients with neuromuscular conditions

Dr Michel Toussaint (Physiotherapist at the Inkendaal Rehabilitation Centre, Belgium)

The position of neuromuscular patients in Shared Decision Making

Dr Anna Ambrosini (ENMC Executive Committee, Head Neuromuscular Research Programmes; Research & Development, Fondazione Telethon, Italy)

Questions and conclusion of the ENMC symposium

Prof. George Padberg (Research Director ENMC)



Dr Ellen Sterrenburg, chair of the ENMC, welcoming the audience to the special ENMC workshop in Vienna.

After the symposium, the ENMC toasted on its 25th anniversary with the participants and symposium speakers.



Prof. Kevin Campbell stepping from the audience to the microphone to express his gratitude to the ENMC:

“ENMC has been an essential element for my research activities and personal career within the neuromuscular field. The ENMC helped me build a strong network with colleagues, and my long-term collaborations with other researchers were initiated at ENMC workshops.”

6 Resources and financial management in 2018

Financial summary 2018

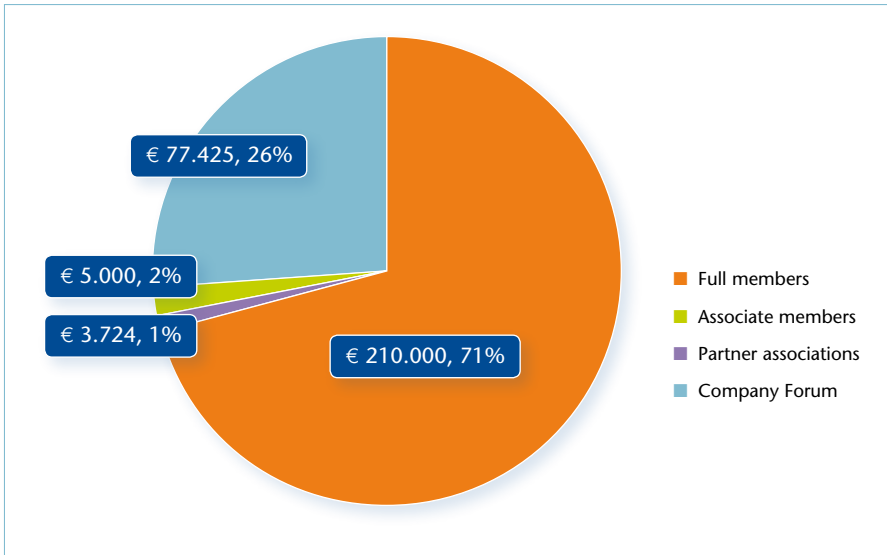
Annual accounts for the year 2018 were compiled in accordance with Guideline C1 for the reporting of small-sized non-profit organisations as published by the Dutch Accounting Standards Board. The financial accounts are drawn up in Euros.

In the summary table below, the overall income and expenses over the year 2018 are shown in comparison with the figures for the financial year 2017.

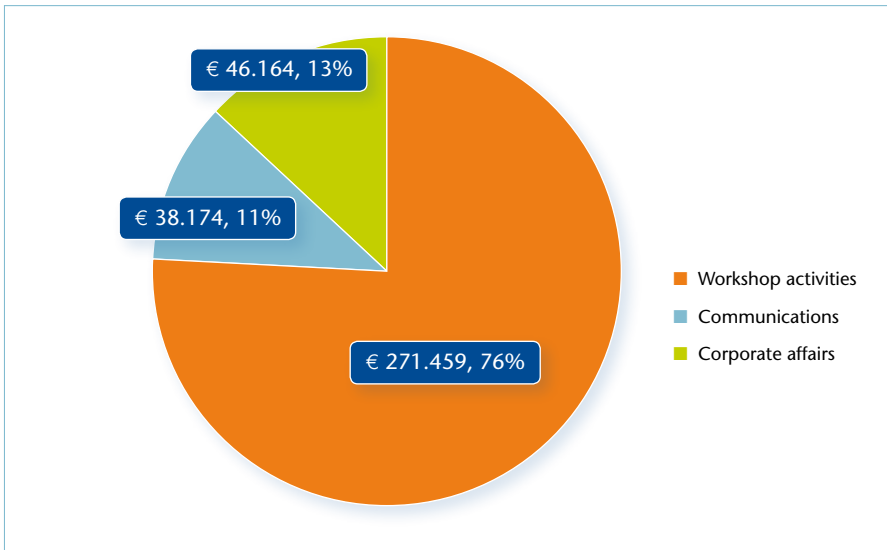
Statement of income and expenses for the year 2018 in comparison with 2017 in Euros (€)		
	2018	2017
INCOME		
Member contributions	210.000	210.000
Associated member contributions	5.000	5.000
Company Forum contributions	77.425	63.957
Other contributions	3.724	32.792
Total income	296.149	311.749
EXPENSES		
Personnel expenses	143.436	149.034
Rental expenses	11.300	11.997
Activity (workshop) expenses	157.814	87.114
Organisational expenses	43.248	40.274
Total operating expenses	355.798	288.419
Operating result	-59.649	23.330
Interest income	193	502
Net result	-59.456	23.832
APPROPRIATION OF RESULTS		
Reserve for 25th Anniversary	-14.848	-8.009
Reserve for additional workshop costs	-48.000	-15.155
Other free reserves	3.392	46.996
CASH AT BANKS ON 31 DECEMBER	507.136	491.595

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

Distribution of income 2018



Distribution of costs 2018



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 2018, please visit the ENMC website.

From left to right: Ms Annelies Zittersteijn and Dr David Hilton-Jones handing over some presents to Prof. George Padberg.



Goodbye from Prof. George Padberg as ENMC Research Director

The term of Prof. George Padberg ended on December 31st 2018 after 5 years of fulfilling the role of ENMC Research Director. The ENMC greatly thanks him for his excellent chairmanship of the Research Committee, for his support and advice to the ENMC and his devotion to the ENMC mission.



7 Governance 2018

The European Neuromuscular Centre (ENMC) was founded as a non-profit organisation on 24 November 1992 under Dutch law. The foundation is supported by financial contributions of nine European patient organisations for neuromuscular disorders and other related organisations. The statutory location is in Baarn, in The Netherlands, in the building of the Dutch Neuromuscular Diseases Patient Association.

7.1 The ENMC Executive Committee

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

Composition of the ENMC Executive Committee on 31 December 2018:

Dr K. Adcock (United Kingdom)
Dr A. Ambrosini (Italy)
Dr I. Meijer (The Netherlands)
Dr A. Méjat (France)
Dr A. von Moers (Vice Chair, Germany)
Dr J. Rahbek (Denmark)
Dr E. Sterrenburg (Chair, The Netherlands)
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 2018:

Prof. Dr G.P. Comi (Italy)
Dr D. Hilton-Jones (United Kingdom)
Prof. Dr H. Jungbluth (United Kingdom)
Prof. Dr P. Laforêt (France)
Dr M. Olivé (Spain)
Prof. Dr G. Padberg (Chair, The Netherlands)
Prof. Dr M.A. Rüegg (Switzerland)
Prof. Dr T. Sejersen (Sweden)
Prof. Dr W. Stenzel (Germany)
Prof. Dr V. Timmerman (Belgium)
Dr N. Voermans (The Netherlands)

7.3 The ENMC Office

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

ENMC Office staff on 31 December 2018:

Dr A. Breukel (Managing Director)
Ms A. Zittersteijn (Operational Manager)
Prof. Dr G. Padberg (Research Director)
Ms M. Edens and Ms L. Verwer (Workshop Assistants)

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

It is thanks to the continuous support of the nine 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

and members of the ENMC Company Forum, we are also able to invite participants from non-ENMC countries and facilitate the attendance of young scientists and patient representatives.

ENMC full and associated members



Finnish Neuromuscular Disorders Association



Deutsche Gesellschaft für Muskelkranke e.V. DGM

Members of the Company Forum



Workshop-specific sponsors



9 Looking forward to 2019 and beyond

In total, ten ENMC workshops are planned to take place in 2019 (see table below). Two review rounds for workshop applications are planned: one in the

spring and one in the autumn. The workshops that are selected at these review rounds will be planned in 2019 and 2020.

Preliminary ENMC programme 2019 (www.enmc.org)

Workshop no./date	Topic	Workshop leaders
Workshop no. 240 25–27 January 2019	The involvement of skeletal muscle stem cells in the pathology of muscular dystrophies	Dr J. Morgan, Prof. K. Patel, Prof. F. Muntoni, Dr G. Butler Browne
Workshop no. 241 15–17 February 2019	Towards a European unifying lab for Kennedy's disease	Dr M. Pennuto, Dr G. Sorarù, Dr L. Greensmith, Dr P.F. Pradat
Workshop no. 242 1–3 March 2019	Diagnosis and management of Juvenile Myasthenia Gravis	Dr P. Munot, Dr J. Palace, Dr E. Niks, Dr S. Robb
Workshop no. 243 22–24 March 2019	Developing guidelines for management of reproductive options for families with maternally inherited mtDNA disease	Prof. J. Poulton, Prof. J. Steffann, Dr J. Burgstaller, Prof. B. McFarland
Workshop no. 244 10–12 May 2019	Neonatal screening of Spinal Muscular Atrophy	Dr E. Tizzano, Dr L. Servais
Workshop no. 246 24–26 May 2019	Protein Aggregate Myopathies	Dr M. Olivé, Dr R. Schröder
Workshop no. 250 6–8 September 2019	Clinical trial readiness in nemaline myopathy caused by mutations in the nebulin and actin (ACTA1) genes	Prof. L. Servais, Prof. C. Wallgren Pettersson, Prof. C. Bönnemann
Workshop no. 247 20–22 September 2019	Muscle Magnetic Resonance Imaging: Implementing muscle MRI as a diagnostic tool for rare genetic myopathy cohorts MRI	Prof. V. Straub, Prof. J. Díaz Manera, Dr G. Tasca, Dr J. Warman Chardon
Workshop no. 248 11–13 October 2019	Myotonic dystrophies: molecular approaches for clinical purposes. Framing a European molecular research network	Dr R. Wansink, Dr G. Gourdon, Prof. B. van Engelen, Prof. B. Schoser
Workshop no. 249 29 November– 1 December 2019	The role of brain dystrophin in muscular dystrophy: Implications for clinical care and translational research	Dr H. Kan, Prof. F. Muntoni, Prof. M. Thangarajh

ENMC publications in 2019

The results of the overall impact of ENMC workshops, analysed by the retrospective impact and bibliometric analysis, will be published in *Neuromuscular Disorders* in 2019. The outcomes will also be summarised in lay language for the general public and supported by interviews with workshop organisers.

Two papers reporting on the outcomes of the 235th ENMC workshop on “the position of the neuromuscular patient in Shared Decision Making” were accepted for publication by the *Journal of Neuromuscular Diseases* and *Orphanet Journal of Rare Diseases*, respectively: one paper will address the patient’s involvement in neuromuscular research, and one will report on the discussions regarding patient’s needs in daily life.

Welcome to our new Research Director Dr Ana Ferreiro

Ana Ferreiro, MD, PhD will become the new ENMC Research Director as of 1st January 2019. We congratulate Ana on her new task within our organisation and look forward working with her. Dr Ana Ferreiro is Research Director at the INSERM “Basic and Translational Myology” laboratory Unité de Biologie Fonctionnelle et Adaptative (BFA), Université Paris, France. She is also a consultant neurologist at one of the ERN centres: The Institut of Myology, Pitié-Salpêtrière Hospital in Paris.

We will be working on themes such as patient participation in ENMC activities and encouragement of young scientists to join the ENMC network. Ana will accompany the ENMC office at several international NMD meetings and at ENMC workshops to meet with you in person.

International conferences in 2019

ENMC representatives will run a booth, present posters and participate in the scientific programme of the following local and international conferences:

- 26–28 March: Myology 2019, Bordeaux, France
- 4–5 April: 12th Annual Neuromuscular Translational Research Conference, Newcastle upon Tyne, UK
- 22–25 June: Peripheral Nerve Society meeting in Genoa, Italy
- 14 September: Muscle Disorders Patient Conference in Veldhoven, The Netherlands
- 2–4 October: Annual Congress of the World Muscle Society in Copenhagen, Denmark
- 10–11 December: TREAT-NMD conference in Leiden, The Netherlands



Dr Ana Ferreiro

Budget for 2019

This table presents the budget forecast for 2019.

Budget 2019 in Euros (€)	Actuals 2018	Budget 2019
INCOME		
Member contributions	210.000	210.000
Associated member contributions	5.000	5.000
Company Forum contributions	77.425	77.436
Other contributions	3.724	5.000
Total income	296.149	297.436
EXPENSES		
Personnel expenses	143.436	149.000
Rental expenses	11.300	11.500
Activity expenses	157.814	137.000
Organizational expenses	43.248	42.800
Total operating expenses	355.798	340.300
Interest income	193	500
NET RESULT	-59.456	-42.364
APPROPRIATION OF RESULTS		
Continuity reserve	-	-
Reserve for 25th Anniversary	-14.848	
Reserve for additional workshop costs	-48.000	-31.000
Correction of negative results	3.392	-11.364



Colophon

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