

The position of neuromuscular patients in Shared Decision Making

Recommendations from ENMC Workshop:

Milan, Italy, January 19-20, 2018

On behalf of the ENMC Executive Committee and the Milan workshop participants

Anna Ambrosini, Alexandra Breukel, Ingeborg Meijer, Alexandre Méjat and Raffaella Willmann

Contents	<i>page</i>
<u>Executive Summary</u>	<u>3</u>
<u>Workshop participants</u>	<u>4</u>
<u>Genetic Diagnosis, Screening and Predictive Testing</u>	<u>5</u>
<u>Transition from Child- to Adulthood</u>	<u>7</u>
<u>Health Care Research</u>	<u>9</u>
<u>Registries and Biobanks</u>	<u>11</u>
<u>Clinical Trial Design</u>	<u>13</u>
<u>Regulatory Issues and Health Technology Assessment</u>	<u>15</u>
<u>References</u>	<u>17</u>
<u>Internet Links</u>	<u>18</u>
<u>Acknowledgements</u>	<u>19</u>
<u>Contact details ENMC</u>	<u>20</u>

Executive Summary

In the field of neuromuscular disorders, engaging patients has since long been recognised as key issue. For patients and patient organisations, it is the time to discuss how and when they want to be engaged in research and health care and how patients want this co-creation process to further develop.

An effective example of the involvement of patient organisations in the neuromuscular research field is the European Neuromuscular Centre (ENMC) itself. The ENMC was co-founded by a group of neuromuscular patient organisations and clinicians to encourage and facilitate communication and collaboration in the field of neuromuscular research. Since then, a structural collaboration began between the ENMC Research Committee, consisting of researchers and clinicians working in the field, and the Executive Committee, consisting of patient organisation representatives. Moreover, ENMC encourages active participation of patients in each of its workshops.

A special workshop hosted by ENMC in Milan to celebrate its 25th anniversary aimed at discussing the level of patient participation in a set of domains considered relevant for the neuromuscular community with key stakeholders. The following topics were chosen for discussion:

1. psycho-social support of families going through the processes of screening and diagnosis
2. transition from child, to adolescent to adult patient
3. healthcare-related research that has major impact on daily life
4. registries and biobanks
5. clinical trial design
6. regulatory and consenting processes

[The concept of *shared decision making* was used throughout the workshop's discussions to characterise the partnership-based identification of the wishes and needs of all stakeholders involved. Although the theory and enactment of *shared decision making* in healthcare are well-described in the literature, comparatively less attention has been devoted to contextualizing questions related to if, when, and how to include patients in decisions within medical research. At the meeting, the "*ladder of participation*" tool served as a model to evaluate the actual and the desired level of patients' involvement in all topics addressed (Ambrosini et al, 2019; Lochmüller et al, 2019). Accordingly, patient's role starts from providing "information" and advice ("consultation"), which are important steps towards the collection of patients' knowledge and engagement if accompanied by an active listening of their voice by the other stakeholders. Higher levels of engagement are represented by the levels of "collaboration" (partnership in a project) and "control" (initiative of a project).

This **White Paper** is based on the outcome of the Milan workshop and, in particular, it reports the consensus reached on specific recommendations for patient organisations and health care professionals, together with key examples analysed during the meeting.

It is a **call to action to all stakeholders to become ambassadors** and promote a cultural change for the direct involvement of people living with a neuromuscular disorder in all aspects of health care and medicine development related to their disease.

This White Paper is intended as a tool for everyone, please feel free to use it in your local organisations and collaborations, where needed. We kindly ask you to disseminate it as much as possible, to the people and organisations in your network and/or country and wherever you consider it pertinent.

Workshop participants

Dr Anna Ambrosini (Italy)
 Dr Dimitrios Athanasiou (Greece)
 Mrs Nathalie Bere (The Netherlands)
 Dr Fabiola Bertinotti (Italy)
 Dr Alexandra Breukel (The Netherlands)
 Mr Filippo Buccella (Italy)
 Mr Nic Bungay (United Kingdom)
 Mrs Caroline Daly (Switzerland)
 Prof. Baziel van Engelen (The Netherlands)
 Mr. Ettore Galluccio (Italy)
 Dr Carsten Gamroth (Germany)
 Prof. Nathalie Goemans (Belgium)
 Mr Gábor Gömöri (Hungary)
 Prof. Mats Hansson (Sweden)
 Mr François Lamy (France)
 Dr Erik Landfeldt (Sweden)
 Dr Mencia de Lemus (Spain)
 Mrs Anne Lennox (United Kingdom)
 Prof. Hanns Lochmüller (Germany, Canada)
 Dr Hank Mansbach (USA)
 Dr Elena Mazzone (Italy)
 Dr Ingeborg Meijer (The Netherlands)
 Dr Alexandre Méjat (France)
 Mrs Anneke Mels (The Netherlands)
 Dr Arpad von Moers (Germany)
 Dr Lucia Monaco (Italy)
 Prof. George Padberg (The Netherlands)
 Dr Holly Peay (U.S.A.)
 Dr Ros Quinlivan (United Kingdom)
 Dr Jes Rahbek (Denmark)
 Dr Marco Rasconi (Italy)
 Mr Michal Rataj (Poland)
 Dr Françoise Salama (France)
 Dr Valeria Sansone (Italy)
 Prof. Ulrike Schara (Germany)
 Prof. Guus Schrijvers (The Netherlands)
 Dr Mike Snape (United Kingdom)
 Dr Ellen Sterrenburg (The Netherlands)
 Prof. Aad Tibben (The Netherlands)
 Mrs Kimberly Trant (U.S.A.)
 Drs Elizabeth Vroom (The Netherlands)
 Dr Raffaella Willmann (Switzerland)
 Dr Maarten de Wit (The Netherlands)
 Mrs Annelies Zittersteijn (The Netherlands)

Genetic Diagnosis, Screening and Predictive Testing

“Knowledge is Power”

Today, easy access to the internet and social media has enabled people to gain detailed information about their specific condition when available. The mutual interaction of all stakeholders involved (geneticist, physician, patients and their families) and the good practice of *shared decision making* in the dialogue between patient and physician are essential to make this information powerful and useful.

Diagnostic or predictive testing together with an open and informative bilateral communication between the patient/family and the physician allow for the promotion of patient autonomy, individually tailored shared decision making and ultimately improvement of the patient’s quality of life.



RECOMMENDATIONS for patient organisations

- Map the best practices for your disease from different countries and share results with the patients and families
- Explore the experiences of organisations in other areas of the rare disease field
- Empower patients by offering training on the challenges of genetic testing/screening programmes in view of available and future therapeutic options
- Identify experts who can and will take the lead-role on specific initiatives
- Set up support groups (face-to-face and/or virtual) and promote peer-to-peer discussion
- Launch surveys to capture patients’ needs and preferences about genetic diagnosis, preclinical screening, predictive testing.



RECOMMENDATIONS for physicians

- Create more dialogue with patient organisations, involve patients or patient representatives before implementing screening
- Explain reasons and timing of the genetic diagnosis/screening, define the type of support that may or may not be on offer
- Set up a diagnosis/screening group involving experts and the disease-specific patient organisations
- Train doctors on the technique of *shared decision making* to improve dialogue and involvement of patients
- Proactively stimulate workshops about this topic.

RECOMMENDATIONS for patients and parents

- Search for specific patient organisations in your country
- Empower yourself by learning about the diagnostic and therapeutic options, learn to ask your doctor(s) the right questions
- Request a *shared decision making* type of dialogue with health care professionals.

Genetic Diagnosis, Screening and Predictive Testing

INSIGHTS

SHARED DECISION MAKING is “... an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences.” [from: Elwin G et al. BMJ 2017]

When *shared decision making* is correctly adopted, outcomes are:

- Knowledge of the available options and their characteristics
- Informed perception of risks towards benefits
- Consideration of the patient’s values and preferences with respect to available options
- Joint decision, reassurance and confidence regarding the decision
- Consideration of barriers and facilitators to put the decision into practice
- Better adherence to the chosen option

THE NEUROMUSCULAR DISEASES’ SCENARIO

The availability of therapeutic options for Duchenne muscular dystrophy and spinal muscular atrophy and the development of gene therapy clinical trials for other neuromuscular disorders urged the implementation of genetic diagnosis and the initiation of newborn screening programmes.

The neuromuscular community is already engaged in addressing these issues and care guidelines have been developed by specialists with the support of patient organisations (see discussion at the workshop and references reported in Ambrosini A et al. OJRD 2019). Further discussion is ongoing addressing disorder-specific needs and characteristics (see for instance the ENMC workshops’ reports: <https://www.enmc.org/download/developing-guidelines-for-management-of-reproductive-options-for-families-with-maternally-inherited-mtdna-disease> and <https://www.enmc.org/download/newborn-screening-in-spinal-muscular-atrophy>).

CASE EXAMPLE discussed at the workshop

The experience of the European Huntington’s disease network (EHDN; <http://www.ehdn.org/>)

The interaction of an EHDN dedicated working group that included family members, genetic counsellors, psychologists, clinical geneticists, neurologists, and laboratory scientists, allowed the development of important recommendations for the predictive genetic test in Huntington’s disease. The recommendations that guide and inform clinical practice are based on current evidence and expertise, and are made to best to serve the needs of individuals and families.

References

MacLeod R et al. Clin Genet 2013.

See paper of Ambrosini A et al. OJRD 2019 for a deeper discussion of Patient involvement in Genetic Diagnosis, Screening and Predictive Testing.

Key references published after January 2018 are added where pertinent as example only and by no means with the intention to be exhaustive.

Transition from Child- to Adulthood

“Growing in competency”

In the process of moving on from children's health care to adult health care, young people with a neuromuscular disease are challenged to become independent and make their own decisions.

As care improves for some diseases, this young adult population is now increasing. However, sometimes, young people reach the transition age without proper preparation for this process, with a limited understanding of their condition and insufficient information to take their own decisions regarding care, treatments and future shaping. This can result in a high rate of non-attendance for routine follow-up appointments, need for disease progression studies and necessary examinations at the care centres.



RECOMMENDATIONS for young patients, parents, carers and patient organisations

- Enable patients to live independently (in the family, at school, at work) and become autonomous adults
- Raise confidence and self-esteem of young patients, involve them in team activities (e.g. team sports) and encourage a network of friends
- Increase awareness of employability of young people with neuromuscular diseases
- Educate carers and parents on the *shared decision making* attitude in dialogues with their the doctor(s)
- Create ambassadors among patients, parents and caregivers to show the value of behavioural changes
- Facilitate support by peers and the patient communities to exchange experiences and information. Use influence and implementation power of organisations like EURORDIS, European Patient Forum, and EUPATI [<https://www.eurordis.org/>; <https://www.eupati.eu/>; <https://www.eu-patient.eu/>].



RECOMMENDATIONS for physicians

- Progressively involve children/young people in decision making and facilitate their conversation with you as physicians (even without parents)
- Implement transition programmes with multidisciplinary teams, involve the future adult neurologist e.g. in an early stage to make an optimal transfer
- Include young people in the design of health care services and in the development of informational/educational material (co-creation)
- Provide unbiased, validated information on diagnosis, all treatment options, sexuality, family planning and life choices
- Apply shared decision making during dialogues at visits
- Use appropriate language: right level of difficulty and “people living with....” instead of “patients with...”
- Focus on life goals instead of disease management only.

Transition from Child- to Adulthood

INSIGHTS

SHARED DECISION MAKING is “... an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences.” [from: Elwin G et al. BMJ 2017]

When *shared decision making* is correctly adopted outcomes are:

- Knowledge of the available options and their characteristics
- Informed perception of risks towards benefits
- Consideration of the patient’s values and preferences with respect to available options
- Joint decision, reassurance and confidence regarding the decision
- Consideration of barriers and facilitators to put the decision into practice
- Better adherence to the chosen option

THE NEUROMUSCULAR DISEASES’ SCENARIO

The improvement of care opportunities and the availability of supporting therapies create a population of young patients with a chronic disease that switch from full parental care to self-management. This transition process is complex and requires good alignment between paediatric and adult medical care, with interdisciplinary cooperation. From the patient’s perspective, the awareness of their own disease and their expectations may change accordingly and need appropriate guidance too.

Several toolkits are available online to inspire patient organisations and provide guidance for enabling children and young people with a chronic condition to acquire the appropriate skills in decision making (see http://www.muscular dystrophyuk.org/assets/0001/6223/Transition_guide_factsheets_web.pdf or Trout et al. Pediatrics 2018).

CASE EXAMPLE discussed at the workshop

A London-based programme for adolescents and young adults with a neuromuscular disorder supported by Muscular Dystrophy UK

Based on the experience of the MDStarnet (USA), the Great Ormond Street and University College Hospitals (London, UK) have developed a transition service for young people with NMD, which includes:

- A seamless service with a clinician based across both adult and paediatric services
- A joint clinic between adult and paediatric teams
- A young persons’ support group led by a clinical psychologist
- Young persons’ open day with talks on employment, university, independent living etc.
- Development of a multi-disciplinary service including one-stop assessments at a neuromuscular complex care centre
- Signposting to a Muscular Dystrophy UK young persons’ group on social media called ‘Trailblazers’

This programme provides young individuals living with a neuromuscular condition and their families with information, coaching and mentorship, and supports teenagers with guidance from health care professionals, parents and peers.

References

- <https://www.muscular dystrophyuk.org/grants/improving-care-for-adults-with-duchenne-muscular-dystrophy/>
- <https://www.enmc.org/download/adults-with-dmd/>

See paper of Ambrosini A et al. OJRD 2019 for a deeper discussion of Patient involvement in Transition from Child- to Adulthood.

Health Care Research

“Health care research requires co-creation”

Involving and empowering patients in health and medical research is increasingly recognised as an important goal to increase the quality and enhance the relevance of health research, ultimately improving legitimacy and applicability of outcomes. However, the level of patient participation in setting the research agenda is still rather limited to consultation or membership in a committee.

A patient research partner is defined as a person with a relevant condition who provides a patient perspective in the research team as an equal collaborator at all stages of the project. Engaging patients in a research agenda setting is only a first step to more enduring, ongoing dialogues between patients and researchers.



RECOMMENDATIONS for patients and patient organisations

- Be aware and address the challenges for patients in *shared decision making* and participation in health care research (personal barriers such as age, communication, skills, or misinformation in the lay communication or social media, etc.)
- Encourage patient-centric research, explore quantifiable patient preferred measurements as new outcome measures
- Promote dedicated funding for patients' involvement in research approaches
- Consider the introduction of patient panels in commissions and advisory boards
- Inform about centres of expertise where patients may receive adequate information
- Consider training programmes provided by organisations like EURORDIS, European Patient Forum, or EUPATI
[<https://www.eurordis.org/>; <https://www.eupati.eu/>; <https://www.eu-patient.eu/>].



RECOMMENDATIONS for clinical researchers

- Reserve more time to set research plans with involvement of patients' opinions
- Base the physician-patient interaction more on the person than on the disease
- Involve patient representatives as collaborative partners from the beginning
- Ensure the commitment of the research centres' leaders
- Involve expert patients able to represent the interests of a community
- Include dedicated funding for the involvement of patient representatives in the research programme in grant applications
- With patients who need mediation, like children or patients unable to speak, establish a way to reflect the patients' and not the carers' needs.

Health Care Research

INSIGHTS

SHARED DECISION MAKING is “... an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences.” [from: Elwin G et al. BMJ 2017]

When *shared decision making* is correctly adopted outcomes are:

- Knowledge of the available options and their characteristics
- Informed perception of risks towards benefits
- Consideration of the patient’s values and preferences with respect to available options
- Joint decision, reassurance and confidence regarding the decision
- Consideration of barriers and facilitators to put the decision into practice
- Better adherence to the chosen option

THE NEUROMUSCULAR DISEASES’ SCENARIO

With the establishment of the European Reference Network for neuromuscular disorders EURO-NMD (<https://ern-euro-nmd.eu/>), a platform is available for a coordinated implementation of health research across Europe where patient engagement is highly encouraged. Patient representatives from experienced patient organisations are present in several NMD platforms, such as the ERN advisory boards, and involved also in writing guidelines for health care management.

ENMC encourages that persons directly involved with a neuromuscular condition participate in its workshops. They are the ‘experts’ with a neuromuscular condition on a day-to-day basis and can share these experiences with researchers and clinicians also to prioritise the research agenda. A toolkit to facilitate patients’ interaction and contribution to the discussion is available online (<https://www.enmc.org/patient-participation/introduction/>).

CASE EXAMPLES discussed at the workshop

The experience of other condition-specific groups in the involvement of patients as research partners

A Special Interest group was set up by the OMERACT initiative to define outcome domains according to patients’ needs for longitudinal studies on Rheumatoid Arthritis.

The James Lind Alliance supports discussions between patients and clinical researchers over the effectiveness of medical interventions.

In the Netherlands, the Dialogue model was established as a guideline on how to consult and integrate the issues of various stakeholders, including patients, in setting the research agenda.

References

- <https://omeract.org/>
- <http://www.jla.nihr.ac.uk/about-the-james-lind-alliance/>
- <https://www.dialogmodel.nl/hulpverleners/en-method/en-using-the-dialogue-model/>

See paper of Ambrosini A et al. OJRD 2019 for a deeper discussion of Patient involvement in Health Research.

Registries and Biobanks

“Supporting research-support tools”

Through the collection and sharing of patients’ data and rare samples, registries and biobanks are invaluable tools for medical (epidemiological) research and for efficient planning of clinical trials. Well-updated registries and biobanks offer researchers the opportunity to study large patient cohorts and gain precious information on disease natural history and pathological mechanisms.

The direct engagement of patients in providing their data facilitates capturing their daily life experience and brings them closer to medical research. Registries and biobanks are good examples of co-creation, where patients who participate bring valuable contribution and promote research programmes that target their needs and expectations. Relevant issues concern patient access to their data, data sharing and open access. Additionally, the question of relationships with industry funding registries and their right or not of control over the data collected should systematically be addressed.



RECOMMENDATIONS for patient organisations

- Actively participate in the setting up and in the governance of registries and biobanks
- Help to raise awareness in the patient community about the value and rights on their own data and samples, both for the scientific community and for patients themselves
- Contribute to the definition of the Informed Consent form in order to ensure lay language and understandable concepts
- Promote feedback to the patient community of results achieved with the use of patients’ data and samples
- Promote alignment of national registries with the respective international efforts, according to the “FAIR” principles, avoiding as much as possible the development of “silos” and promoting data sharing and open access
- Ensure that the data collected reflects all the aspects of the disease that are relevant to patients
- Define ethical principles of sharing patient data with pharmaceutical industry.



RECOMMENDATIONS for researchers

- Recognise patients who donate data and/or samples as partners in research
- Commit to report back to data providers results derived from registries and biobanks, in the form of regular newsletters and updates, even if a project is discontinued and results are not published
- Collect registry information that reflects the needs and priorities for patients as identified by them
- Engage patient representatives in the definition of the Informed Consent form
- Make clear the implications of donating samples or clinical data to biobanks and registries in all communication to patients (i.e. possible long times before research delivers results, need to keep data updated, worldwide use of anonymised samples and data, sharing of data with industry, taking into account personal data protection and privacy regulation)
- Adopt FAIR principles, by avoiding data silos and promoting data sharing and open access
- Define ethical principles of sharing patient data with pharmaceutical industry.

Registries and Biobanks

INSIGHTS

FAIR PRINCIPLES

Patients who provide their clinical information and specimens to registries and biobanks want to be reassured that these are accessible to the entire research community as rapidly as possible and be used in the best way to promote understanding of their disease and development of therapies.

The FAIR principles provide guidance and good practices for data stewardship. FAIR stands for the 4 major categories of requisites for data management, which are: Findability, Accessibility, Interoperability and Reusability.

[Mascalzoni et al. Eur J Hum Genet. 2015; Wilkinson MD et al. Nature Sci Data 2016; Boeckhout M et al. Eur J Hum Genet 2018]

THE NEUROMUSCULAR DISEASES' SCENARIO

The TREAT-NMD project, which was launched in 2007, contributed to reduce fragmentation and harmonise previous efforts of neuromuscular registries and biobanks. At the same time, it promoted the active engagement of patients and patient organisations in the governance of these research tools.

Nowadays different types of registries are developed and are part of the Treat-NMD Global Registry infrastructure, which has been acknowledged as "IRDiRC (International Rare Diseases Research Consortium) recognised resources" (<https://treat-nmd.org/what-is-a-patient-registry/>). Similarly, the biobanks' network «Eurobiobank» participated in Treat-NMD and RD-Connect (<https://rd-connect.eu/>) projects and is now recognised as referring network of rare disease biobanks aligned with the FAIR principles (<http://www.eurobiobank.org/>).

In May 2019, the Patient Advisory Board of the EURO-NMD ERN proposed a new model for the EURO-NMD ERN Registry Hub, based on the FAIR principles (<https://ern-euro-nmd.eu/registries-position-paper-issued-by-patient-advisory-board/>).

CASE EXAMPLES discussed at the workshop

Role of patients in the governance of patient- or clinician-driven registries and biobanks

Registries may have different designs and be based on data reporting performed directly by patients/their families or with clinical data collected and entered by clinicians (dual reporting registries).

Several were discussed during the Milan workshop, ranging from the experience of TREAT-NMD registries to dual reporting models, such as the UK myotonic dystrophy registry or the Italian neuromuscular registry, highlighting strengths and limitations of the different models and the role of patient organisations in the governance. The experiences of the Italian network of biobanks and Eurobiobank were also discussed.

References

Ambrosini A et al. OJRD, 2018
<https://newcastle-muscle.org/uk-myotonic-dystrophy-registry/>
http://www.registronmd.it/?page_id=461
<http://biobanknetwork.telethon.it/>

See paper of Lochmüller et al. JNMD 2019 for a deeper discussion of Patient involvement in Registries and Biobanks.

Key references published after January 2018 are added where pertinent as example only and by no means with the intention to be exhaustive.

Clinical Trial Design

“Partners in research”

Having the patient voice throughout the design and execution of a clinical trial is not only feasible, it should be logical and natural. The involvement of people living with a neuromuscular disease as experts should happen in a proactive way from the beginning of the discussion on trial design throughout the conduct of the study and the feedback to patients on the outcomes.

The final goal of a co-creation process in clinical trials is to set up a sustainable patient-health care professionals-partnership to include patients’ perspectives on feasibility and outcomes of a trial, with a clear communication strategy at different levels, from management of expectations to sharing of results. This approach contributes to higher retention levels throughout the study and higher satisfaction of the involved patients.



RECOMMENDATIONS for patient organisations and patient representatives

- Take a leading role in ensuring that more (several) patients are empowered by offering education and coaching for a competent collaboration in clinical trial design and execution
- Promote participation of patients and patient advocates in EURORDIS, EUPATI or European Patient Forum patient courses or related activities [<https://www.eurordis.org/>, <https://www.eupati.eu/>, <https://www.eu-patient.eu/>]
- Avoid always having the same individuals involved in all projects and committees
- Bring into the research activities the community’s points of view and not individual concerns. Collect community point of view by surveys, interviews, input from disease-specific workgroups etc.
- Contribute to the definition of the Informed Consent form in order to ensure lay language and understandable concepts.



RECOMMENDATIONS for clinical trial leaders

- Involve patient representatives in all main phases of a study (trial design, recruitment, preparation of the informed consent, amendments, dissemination of information on trial recruitment, monitoring and results)
- Provide clear explanations to patient organisations and their representatives that take part in the discussions on the scientific rationale of the trial and rigor needed
- Commit to report back to patient organisations and trial participants the results of the study, even if negative or discontinued
- Allocate part of the clinical trial budget and plan time for the interaction with patients and patient organisations, conduct of surveys, evaluation of preferences, to incorporate in the trial design the patients’ view.

Clinical Trial Design

INSIGHTS



The Research and Development of a new drug follows several different phases and is a long and costly process. The partnership between researchers from both academia and pharmaceutical industry, clinicians and patient organisations/representatives may occur at different stages and levels of involvement, depending on the interest and the required expertise [Figure modified from: Geissler J et al. Therapeutic Innovation & Regulatory Science 2017].

THE NEUROMUSCULAR DISEASES' SCENARIO

During the last decade patient organisations actively contributed to improve study design for the testing of innovative therapies, for instance by favouring the collection of natural history data or collaborating in the design of more effective outcome measures. The neuromuscular community should capitalise on this experience and exploit it more to promote the development of new therapeutics for neuromuscular disorders.

CASE EXAMPLES discussed at the workshop

The OPTIMISTIC study; a virtuous partnership with patients for design and conduct of the study

The OPTIMISTIC (Observational Prolonged Trial In Myotonic dystrophy type 1 to Improve Quality of Life-Standards, a Target Identification Collaboration) trial was designed to compare cognitive behavioural therapy plus graded exercise against standard patient management regimes for myotonic dystrophy type 1. "The consistent patient involvement in all phases of trial design led to a constructive collaboration, high compliance and appropriate readouts that increased the value of the trial." (Prof. Baziel van Engelen, trial coordinator, Radboud University, Nijmegen, The Netherlands).

The PREFER PROJECT was set up to develop methods to drive surveys. Stakeholders can make use of this methodology to set up well-planned surveys to assess the patient and economical risk-benefit of a new medicine in the areas of rheumatology, oncology and neuromuscular disorders.

References

- <https://www.myotonic.org/optimistic-view-dm1>
- <https://www.imi-prefer.eu/>

See paper of Lochmüller et al. JNMD 2019 for a deeper discussion of Patient involvement in Clinical Trial Design.

Regulatory Issues and Health Technology Assessment

“Working together to make therapies accessible”

Direct contact with regulatory agencies occurs at different stages in the development of medicines, from design of trial protocols, including patient related outcome measures, to pre-approval, evaluation and post-approval phases, and involve both health care professionals and patient representatives.

Experiences include involvement in discussions on risk-benefits analyses within the assessment of marketing authorisation applications for new therapeutics, a demanding task that implies important responsibilities of the neuromuscular community.



RECOMMENDATIONS for patient organisations

- Take a leading role in ensuring that (several) patients are empowered for competent collaboration in regulatory discussions and that they are able to bring in the community’s concerns, for instance by promoting expert patients’ courses or other initiatives
- Monitor that expert patients are involved at the different stages of the regulatory processes (from clinical phase I until marketing authorisation and clinical phase IV)
- Lobby with the other stakeholders and payers for the involvement of expert patients in the different health economics and costs discussions.

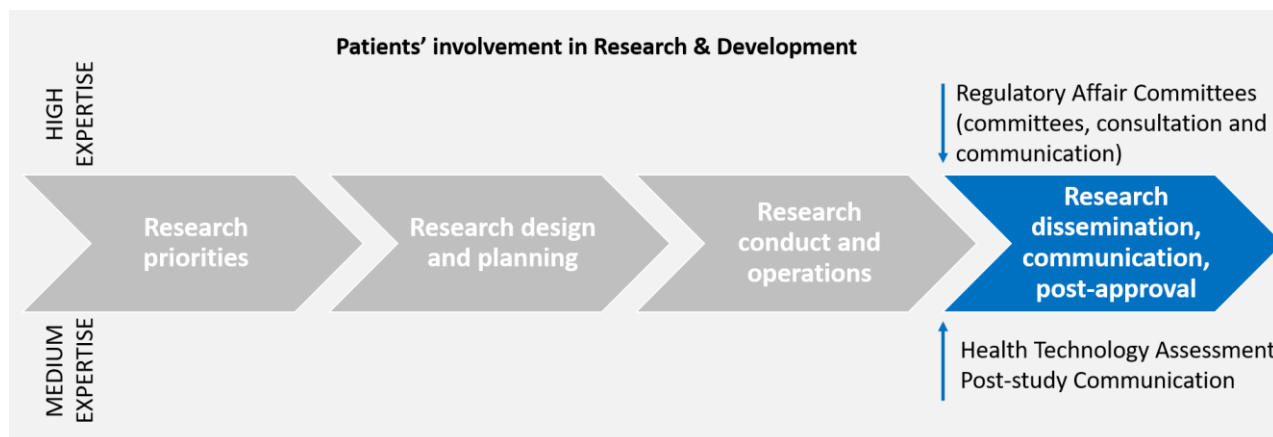


RECOMMENDATIONS for clinicians and health care/regulatory professionals

- Promote involvement of patient organisations and patient representatives in the regulatory review process for new treatments
- Make sure that patient organisations and patient representatives are involved in the national consultations for pricing and reimbursement of approved drugs
- Involve patient representatives to address Health Technology Assessment and healthcare costs derived from the chronic nature of neuromuscular conditions and related comorbidities and psychosocial requirements
- Make use of patient preferences surveys in regulatory reviews
- Incorporate results of patient preferences surveys in educational programmes for expert patients.

Regulatory Issues and Health Technology Assessment

INSIGHTS



With therapies receiving marketing authorisation and ongoing discussions on pricing and reimbursements, new fields arise where active patients’ involvement and consideration of disease specific needs and expectations are requested. Their involvement can be at different levels, depending on the interest and the required expertise [Figure modified from: Geissler J et al. Therapeutic Innovation & Regulatory Science 2017].

THE NEUROMUSCULAR DISEASES’ SCENARIO

For a few neuromuscular disorders innovative therapies are already reality and the work of patient organisations and expert patients has been instrumental during the consultation process of Regulatory Authorities to inform on what matters most to patients and families, their health priorities and burden in the daily life. With the advent of new therapeutics for more and more neuromuscular conditions in the near future, it is of utmost importance preparing the community to support the decision making process at all levels.

CASE EXAMPLES discussed at the workshop

Meetings with the regulatory Authorities; the experience of neuromuscular patient organisations

Patient panels exist in the European Medicine Agency (EMA) and Federal Drug Association (FDA) review processes throughout all phases of drug development to bring in the patient’s perspective. “For the EMA and the FDA, there is no question of the importance of patient engagement and the added value it brings to the regulation of medicinal products by promoting the development of treatment options that better reflect their needs and priorities.”

The pro-active role of the Dutch Muscle Disorders Association in the discussions with the Health Authority regarding the reimbursement of Genzyme’s medicine for Pompe’s disease.

The role of SMA Europe and local patient organisations in the authorization of Nusinersen (Spinraza) in SMA patients above 12 years of age.

References

Mavris M et al. *Nature Reviews Drug Discovery* 2019

See paper of Lochmüller et al. JNMD 2019 for a deeper discussion of Patient involvement in Regulatory Issues and Health. Technology Assessment.

Key references published after January 2018 are added where pertinent as example only and by no means with the intention to be exhaustive

Outcomes and consensus from the ENMC workshop on “The position of the neuromuscular patient in shared decision making” 19-20th January 2018. www.enmc.org

References

- Ambrosini A**, Calabrese D, Avato FM, Catania F, Cavaletti G, Pera MC, et al. The Italian neuromuscular registry: A coordinated platform where patient organisations and clinicians collaborate for data collection and multiple usage. *Orphanet J Rare Dis* 2018;13(1):176
- Ambrosini A**, Quinlivan R, Sansone V, Meijer I, Schrijvers G, Tibben A, Padberg G, de Wit M, Sterrenburg E, Mejat A, Breukel A, Rataj M, Lochmüller H, Willmann R and on behalf of the 235th ENMC workshop study group; “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. *Orphanet J Rare Dis* 2019, 14:1-12
- Boeckhout M**, Zielhuis GA and Bredenoord AL. The FAIR guiding principles for data stewardship: fair enough? *Eur J Hum Genetics* 2018 26; 931-936
- Elwyn G**, Durand M, Song J, Aarts J, Barr PJ, Berger Z, Cochran N, Frosch D, Galasiński D, Gulbrandsen P, Han PKJ, Härter M, Kinnerley P, Lloyd A, Mishra M, Perestelo-Perez L, Scholl I, Tomori K, Trevena L, Wittman HO, van der Weijden T; A three-talk model for shared decision making: multistage consultation process. *BMJ* 2017;359:j4891
- Geissler J**, Ryll B, di Priolo SL and Uhlenhopp M; Improving Patient Involvement in Medicines Research and Development: A Practical Roadmap. *Therapeutic Innovation & Regulatory Science* 2017 51 (5), 612-619
- Lochmüller H**, Ambrosini A, van Engelen B, Hansson M, Tibben A, Breukel A, Sterrenburg E, Schrijvers G, Meijer I, Padberg G, Peay H, Monaco L, Snape M, Lennox A, Mazzone E, Bere N, de Lemus M, Landfeldt E and Willmann R on behalf of the 235th ENMC workshop study group; 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*, 2019, 6:161–172
- MacLeod R**, Tibben A, Frontali M, Evers-Kiebooms G, Jones A, Martinez-Descales A, Roos RA; Editorial Committee and Working Group ‘Genetic Testing Counselling’ of the European Huntington Disease Network. *Clinical Genetics*, 2013, 83(3):221-31
- Mascalzoni D**, Dove ES, Rubinstein Y, Dawkins HJ, Kole A, McCormack P, Woods S, Riess O, Schaefer F, Lochmüller H, Knoppers BM, Hansson M. International Charter of principles for sharing bio-specimens and data. *Eur J Hum Genet*. 2015 Jun;23(6):721-8.
- Mavris M**, Furia Helms A, Bere N; Engaging patients in medicines regulation: a tale of two agencies; *Nature Reviews Drug Discovery* 2019; Vol. 18, Issue 12, pages 885-886
- Trout C**, Case L, Clemens P, McArthur A, Noritz G, Ritzo M, Wagner K, Vroom E and Kennedy A; A Transition Toolkit for Duchenne Muscular Dystrophy. *Pediatrics* 2018, 142(Suppl 2):S110-S117
- Wilkinson MD**, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, et al. The FAIR Guiding principles for scientific data management and stewardship. *Nature Sci Data* 2016;3:160018

Internet Links

- <http://biobanknetwork.telethon.it/>
- <https://www.dialogmodel.nl/hulpverleners/en-method/en-using-the-dialogue-model/>
- <http://www.ehdn.org/>
- <https://www.enmc.org/download/adults-with-dmd/>
- <https://www.enmc.org/download/developing-guidelines-for-management-of-reproductive-options-for-families-with-maternally-inherited-mtdna-disease>
- <https://www.enmc.org/download/newborn-screening-in-spinal-muscular-atrophy>
- <https://www.enmc.org/patient-participation/introduction/>
- <http://www.eurobiobank.org/>
- <https://ern-euro-nmd.eu/>
- <https://ern-euro-nmd.eu/registries-position-paper-issued-by-patient-advisory-board/>
- <https://www.eupati.eu/>
- <https://www.eu-patient.eu/>
- <https://www.eurordis.org/>
- <https://www.imi-prefer.eu/>
- <http://www.jla.nihr.ac.uk/about-the-james-lind-alliance/>
- http://www.musculardystrophyuk.org/assets/0001/6223/Transition_guide_factsheets_web.pdf
- <https://www.musculardystrophyuk.org/grants/improving-care-for-adults-with-duchenne-muscular-dystrophy/>
- <https://www.myotonic.org/optimistic-view-dm1>
- <https://newcastle-muscle.org/uk-myotonic-dystrophy-registry/>
- <https://omeract.org/>
- <https://treat-nmd.org/what-is-a-patient-registry/>
- http://www.registronmd.it/?page_id=461
- <https://rd-connect.eu/about-rd-connect/>

Acknowledgements

We thank the following patient organisations for their help in local management of this meeting in Milan and the co-sponsor for helping to cover travels of many of the participants:



The ENMC Executive Committee organised the 25th Anniversary ENMC workshop in Milan with two specialists who are greatly thanked for all their efforts in initiating, organising and chairing of the two workshop days:

Prof. Hanns Lochmüller (Canada, Germany)

Prof. Aad Tibben (The Netherlands)

We also would like to thank the workgroup leaders, who prepared for and steered the discussions on each of the six domains during the workshop:

Prof. Baziel van Engelen (The Netherlands)

Prof. Mats Hansson (Sweden)

Prof. Hanns Lochmüller (Canada, Germany)

Dr Ros Quinlivan (United Kingdom)

Dr Valeria Sansone (Italy)

Prof. Aad Tibben (The Netherlands)

ENMC full and associated members are greatly thanked for their continuous support of the ENMC:

FONDAZIONE



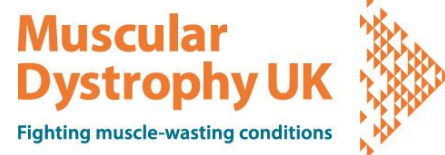
Finnish Neuromuscular Disorders Association



Deutsche Gesellschaft für
Muskelkranke e.V. DGM



MUSKELSVINDFONDEN



European Neuromuscular Centre (ENMC)

Lt. Generaal van Heutszlaan 6

3743 JN Baarn

The Netherlands

00 31 35 5480481

www.enmc.org

enmc@enmc.org

