European
Reference
Network
for rare or low prevalence
complex diseases

Network
Neurological Diseases
(ERN-RND)

European Reference Network for Rare Neurological Diseases – ERN-RND

ERN-RND Information Brochure

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Diffusion:	ERN-RND members

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Summary and objectives

More than 500,000 people in the European Union suffer from a rare neurological disease (RND) which can sometimes take months or even years to diagnose correctly and for which often no treatment is available. This is an extremely challenging and stressful situation, often referred to as a “diagnostic odyssey”, patients and their families have to go through until they get the correct diagnosis. For that purpose, the European Reference Network for Rare Neurological Diseases (ERN-RND) was set up in 2017 with 23 other networks by the European Commission with the overall aim of supporting patients with rare neurological diseases across Europe in getting a faster diagnosis and access to the right treatment and care. This is achieved by connecting healthcare professionals in Europe and enabling the sharing of knowledge and expertise through the Clinical Patient Management System (CPMS), a secure online platform where clinicians discuss a patient’s case with European colleagues and at organised meetings. The ERN-RND is a virtual network made of healthcare professionals, European Patient Advocacy Groups (ePAGs) representatives and researchers located across Europe. It has 31 members in 13 European countries.

The objectives of the ERN-RND are:

1. To significantly increase the overall percentage of RND patients with a final diagnosis
2. To improve and harmonise care of RND patients across the EU
3. To develop, share and implement care pathways and guidelines for all RND groups represented in ERN-RND
4. To support ERN-RND members in designing, implementing and supervising RND training and capacity building activities at the level of member states and of the network.
5. To develop a comprehensive and data based European RND cohort to better understand these conditions and thus improve their management and help developing and testing treatments
6. To define minimum quality and interoperability criteria for data in RND registries allowing data exchange between local registries and use of data from different registries for one clinical trial

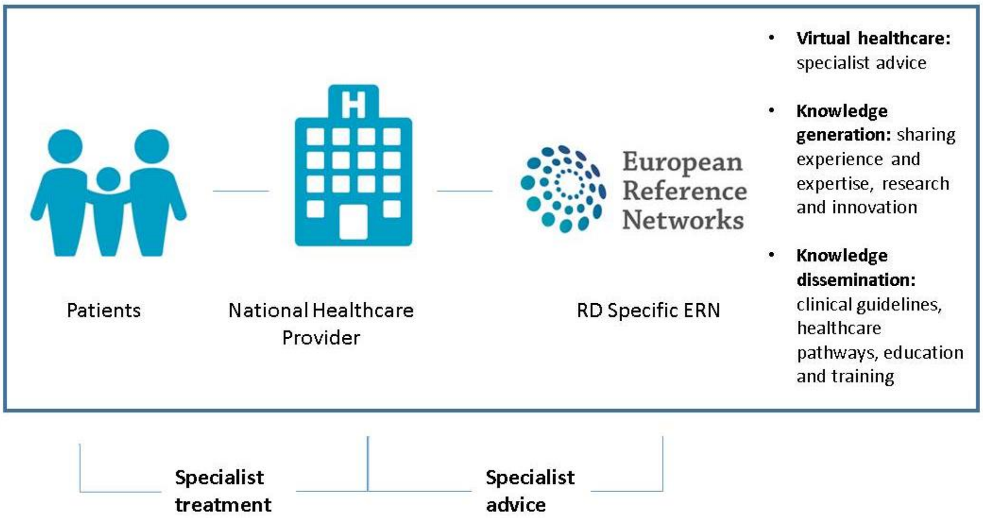

Figure 1: How ERNs work

ERN-RND provides care for approximately 35.000 patients per year (85% adults, 15% paediatric patients), of which 5.300 are new patients. The Disease Groups covered by the ERN-RND are as follows:

- Cerebellar Ataxia and Hereditary Spastic Paraplegias (HSPs)
- Chorea and Huntington’s Disease (HD)
- Dystonias, Neurodegeneration with Brain Iron Accumulation (NBIA) and Paroxysmal Disorders
- Frontotemporal Dementia (FTD)
- Leukodystrophies
- Atypical Parkinsonism: Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP) and Genetic Parkinson’s Disease (genetic PD)

Figure 2 shows the distribution of patient numbers within the different Disease Groups represented in the ERN-RND.

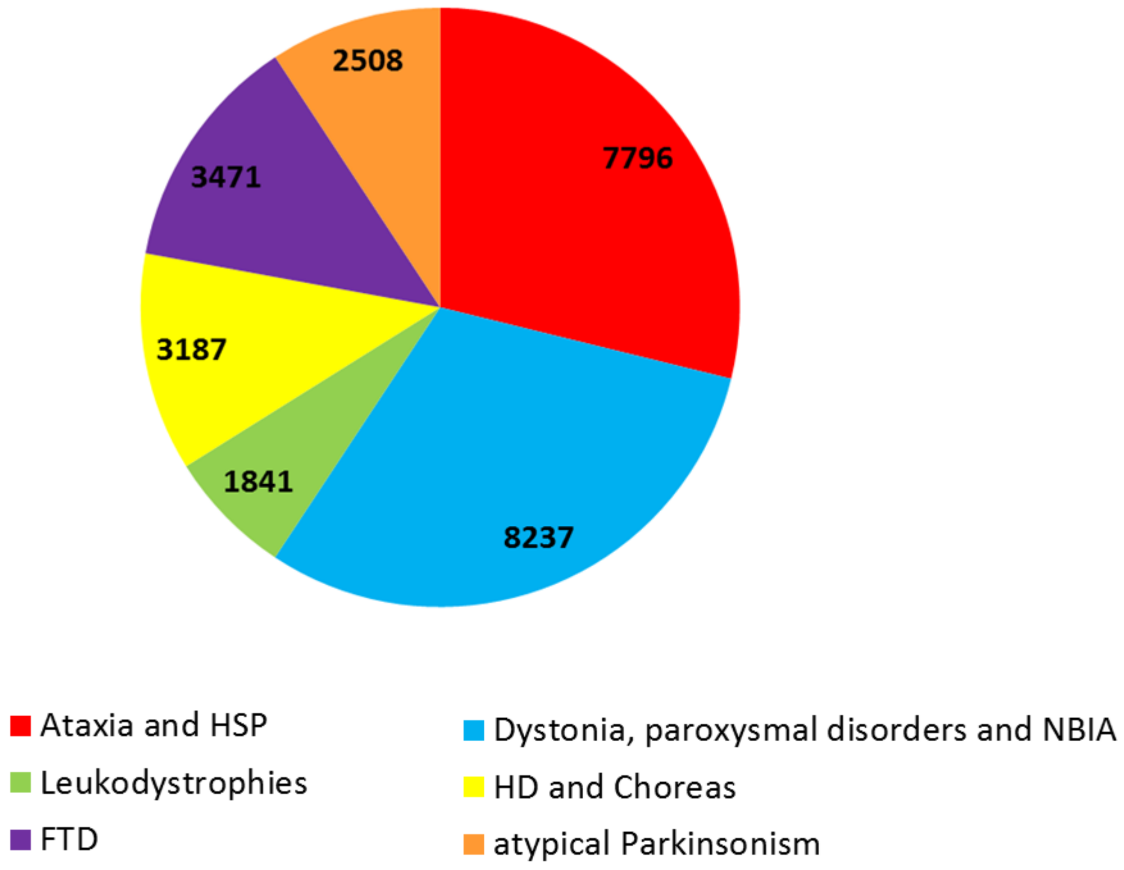

Figure 2: Number of annual patients in the ERN-RND

ERN-RND expert centres

AOU Siena, Italy
Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor, France: Reference centre for Huntington's disease
Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière, France: Reference centre for rare dementias
Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière, France: Reference Centre for Rare Diseases 'Neurogenetics'
Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré, France: Reference centre for Leukodystrophies
CHU de Bordeaux, France: Reference centre for MSA
CHU de Toulouse: Reference centre for MSA
Erasmus MC: University Medical Center Rotterdam, Netherlands,
Foundation IRCCS neurological institute Carlo Besta – Milan, Italy
General University Hospital in Prague, Czech Republic
Hospital Clínic i Provincial de Barcelona y Hospital de Sant Joan de Déu, Spain
Hospital Universitari Vall d'Hebron, Spain
IRCCS Clinical Institute Humanitas – Rozzano, Italy
Klinikum der Universität München, Germany
Motol University Hospital, Czech Republic
Pediatric hospital Bambino Gesù, Rome, Italy
Semmelweis University, Hungary
Stichting Katholieke Universiteit, doing business as Radboud University Medical Center Nijmegen, Netherlands
Universitätsklinikum Bonn, Germany
Universitätsklinikum Schleswig-Holstein, Germany
Universitätsklinikum Tübingen, Germany
Universitätsklinikum Ulm, Germany
Université libre de Bruxelles, Belgium
University College London Hospitals NHS Foundation Trust, United Kingdom
University Hospital in Krakow, Poland
University Hospitals Leuven, Belgium
University Medical Center Groningen, Netherlands
University Medical Centre Ljubljana, Slovenia
University Neurological Hospital “St. Naum” Sofia, Bulgaria
University of Pécs, Hungary
Vilnius University Hospital Santariškių Klinikos, Lithuania
VU University Medical Center Amsterdam, Netherlands

Designated ERN-RND affiliated partners

Pauls Stradins Clinical University Hospital, Riga Latvia
Oulu University Hospital (OUH), Finland
Tartu University Hospital, Estonia
National Coordination Hub, Mater Dei Hospital (MDH), Malta
Center for Rare Movement Disorders / Dpt. of Neurology, Medical University Innsbruck, Austria
University Hospital Cente Zagreb, University Department of Neurology, Croatia
Aarhus Universitetshospital, Denmark
Center for Pediatric Rare Neurological Diseases / Dpt. of Pediatrics, Medical University of Vienna, Austria
Centre Hospitalier du Luxembourg

Affiliated partners of ERN-RND are healthcare providers that can only come from a country not yet represented by a full member in the network and which are allocated by their respective member state. More information about affiliated partners can be found on the European Commission's website here:
https://ec.europa.eu/health/ern/board_member_states_en

Picture 1: ERN-RND members at the Annual Meeting 2019 in Siena, Italy

Achievements

- ERN-RND has collected and generated knowledge to improve care of patients with RND. These disease knowledge documents include:
    - Diagnostic flowcharts
    - Disease scales
    - Therapeutic algorithms
    - Guidelines endorsed by the ERN-RND

Respective documents can be found on the ERN-RND's website here: http://www.ern-rnd.eu/disease-knowledge-hub

- ERN-RND has established a relationship with EMA – Trial readiness and registry workshop on 18 February 2019 in Amsterdam, the Netherlands

Additional ongoing projects include:

- Development of therapeutic algorithms for hereditary spastic paraplegia
- Consensus document on myoclonus dystonia
- Guideline development for metachromatic leukodystrophies

Furthermore, ERN-RND participates in several collaborative projects with professional societies, such as:

- the European Academy for Neurology (EAN): "development of methodology for preparing guidelines for RND" and
- educational webinar series for RND as well as with
- the European Brain Council: "the Value of Treatment Project"

Structure of the ERN-RND

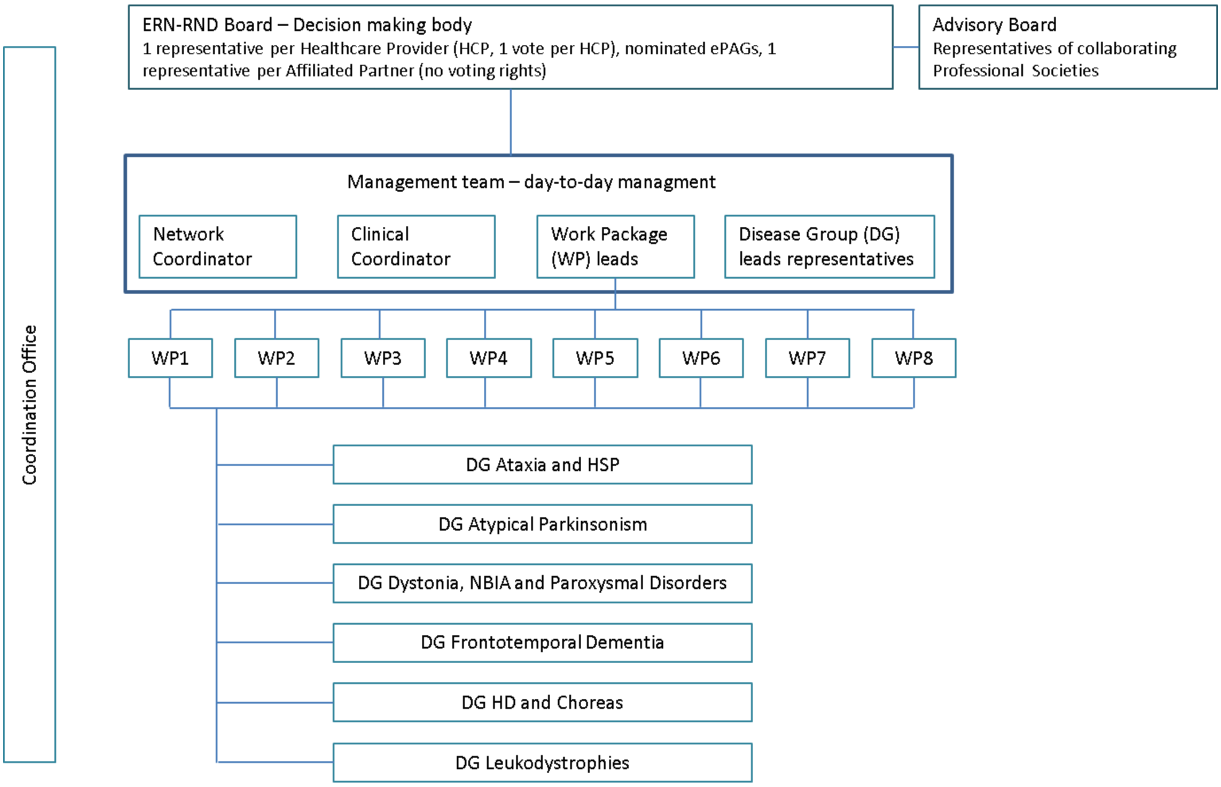

Figure 3: ERN-RND organisational structure

ERN-RND Board

The ERN-RND Board is responsible for strategic decisions and for monitoring the activities of the network. It is the main decision body and is chaired by the network coordinator. The membership of the Board includes individual Health Care Provider (HCP)/Expert centre leads (or their nominated deputies) and the nominated ePAG (European Patient Advocacy Groups) representatives. Affiliated partners will participate in the Board meetings, but will not have any voting rights. The Board members meet twice a year.

The full list of Board members can be found below:

Board member	HCP
Massimo Pandolfo	Université libre de Bruxelles, Belgium
Chantal Depondt	Université libre de Bruxelles, Belgium
Rik Vandenberghe	University Hospitals Leuven, Belgium
Elena Chorbadgieva	University Neurological Hospital “St. Naum” Sofia, Bulgaria
Jiri Klempir	General University Hospital in Prague, Czech Republic
Evzen Ruzicka	General University Hospital in Prague, Czech Republic
Jaroslav Jerabek	Motol University Hospital, Czech Republic
Elena Zumrova	Motol University Hospital, Czech Republic
Wassilios Meissner	CHU de Bordeaux, France

Anne-Catherine Bachoud-Lévi	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor: Reference centre for Huntington's disease, France
Odile Boespflug	Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré: Reference centre for Leukodystrophies, France
Patrick Aubourg	Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré: Reference centre for Leukodystrophies, France
Isabelle le Ber	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière: Reference centre for rare dementias, France
Bruno Dubois	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière: Reference centre for rare dementias, France
Alexandra Durr	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière: Reference Centre for Rare Diseases 'Neurogenetics', France
Claire Ewencyk	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière: Reference Centre for Rare Diseases 'Neurogenetics', France
Anne Pavy-Le Traon	CHU de Toulouse, France
Olivier Rascol	CHU de Toulouse, France
Holm Graessner	Universitätsklinikum Tübingen, Germany
Ludger Schöls	Universitätsklinikum Tübingen, Germany
Thomas Klockgether	Universitätsklinikum Bonn, Germany
Sebastian Paus	Universitätsklinikum Bonn, Germany
Alexander Münchau	Universitätsklinikum Schleswig-Holstein, Germany
Sinem Tunc	Universitätsklinikum Schleswig-Holstein, Germany
Thomas Klopstock	Klinikum der Universität München, Germany
Bernhard Landwehrmeier	Universitätsklinikum Ulm, Germany
Jan Lewerenz	Universitätsklinikum Ulm, Germany
Maria Judit Molnar	Semmelweis University, Hungary
Zoltan Grosz	Semmelweis University, Hungary
Norbert Kovacs	University of Pécs, Hungary
Hadzsiev Kinga	University of Pécs, Hungary
Alberto Albanese	IRCCS Clinical Institute Humanitas – Rozzano, Italy
Stefania Lalli	IRCCS Clinical Institute Humanitas – Rozzano, Italy
Caterina Mariotti	Foundation IRCCS neurological institute Carlo Besta – Milan, Italy
Enrico Bertini	Pediatric hospital Bambino Gesù, Rome, Italy
Ginevra Zanni	Pediatric hospital Bambino Gesù, Rome, Italy
Antonio Federico	AOU Siena, Italy
Maria Teresia Dotti	AOU Siena, Italy
Algirdas Uktus	Vilnius University Hospital Santariškių Klinikos, Lithuania
Nicole Wolf	VU University Medical Center Amsterdam, Netherlands
Marina de Koning-Tijssen	University Medical Center Groningen, Netherlands
Tom de Koning	University Medical Center Groningen, Netherlands
Michel Willemsen	Stichting Katholieke Universiteit, doing business as Radboud University Medical Center Nijmegen, Netherlands

Bart van de Warrenburg	Stichting Katholieke Universiteit, doing business as Radboud University Medical Center Nijmegen, Netherlands
John van Swieten	Erasmus MC: University Medical Center Rotterdam, Netherlands,
Janne Papma	Erasmus MC: University Medical Center Rotterdam, Netherlands,
Harro Selar	Erasmus MC: University Medical Center Rotterdam, Netherlands,
Joanna Pera	University Hospital in Krakow, Poland
Borut Perterlin	University Medical Centre Ljubljana, Slovenia
Dario Ortigozo Escobar	Hospital Clínic i Provincial de Barcelona y Hospital de Sant Joan de Déu, Spain
Maria J Marti	Hospital Clínic i Provincial de Barcelona y Hospital de Sant Joan de Déu, Spain
Alfons Macaya	Hospital Universitari Vall d'Hebron, Spain
Josep Gamez	Hospital Universitari Vall d'Hebron, Spain
Paola Giunti	University College London Hospitals NHS Foundation Trust, United Kingdom
Kailash Bhatia	University College London Hospitals NHS Foundation Trust, United Kingdom
Cathalijne van Doorne	ePAG rep
Mary Kearney	ePAG rep

Management team

The management team is responsible for the management of the ERN-RND. It comprises the network coordinator, the clinical coordinator, the Work Package (WP) leads and representatives of the Disease Group (DG) leads. For the names of the Work Package and Disease Group leads, please see below.

ERN-RND coordination office

The ERN-RND coordination office is comprised of the network coordinator, clinical coordinator, project manager, CPMS manager, communication manager and administrative help. The network coordinator will line manage and interact with the coordination office on a daily basis by monitoring overall activities, liaising with members and external organisations as well as taking key strategic decisions . The project manager will be responsible for administrative tasks which ensure the smooth day-to-day coordination of the network such as the coordination of meetings, organisation of the annual meeting, communication with stakeholders, dissemination of outputs and gathering and collating of monitoring data for reporting and presentation.

The CPMS panel manager and helpdesk will be responsible for most things related to the CPMS which include providing training on how to use the CPMS, organising CPMS case discussions with ERN-RND members and liaising with the European Commission in regards to technical aspects of the system. Finally, the communication manager is responsible for the updating of information on the ERN-RND website, the creation of the newsletter and dissemination of information through social media channels.

Name	Role	Email address
Holm Graessner	Coordinator	holm.graessner@med.uni-tuebingen.de
Ludger Schöls	Clinical coordinator	ludger.schoels@uni-tuebingen.de
Carola Reinhard	Project manager	carola.reinhard@med.uni-tuebingen.de
Sanja Hermanns	CPMS panel manager and helpdesk; Training	sanja.hermanns@med.uni-tuebingen.de
Alicia Brunelle	Communication	alicia.brunelle@med.uni-tuebingen.de

ERN-RND European Patient Advocacy Group Representatives (ePAGs)

EURORDIS, the European umbrella organisation of patient organisations and a non-profit alliance of 798 rare disease patient organisations, has established a European Patient Advocacy Group (ePAG) for each ERN disease grouping. Patient organisations can become ePAG member organisations and patients can become ePAG representatives.
The ERN-RND ePAG representatives are as follows:

ePAG name	Patient organisation
Amanda Rose	Rare Dementia Support
Astri Arnesen	European Huntington Association
Cathalijne van Doorne	Euro-ataxia
Lori Renna Linton	Euro-HSP
Lubomír Mazouch	Czech Association of Atypical Parkinsonian Syndromes
Marek Parkovic	AHC 18 OLUS e.V.
Mary Kearney	Friedreich’s Ataxia Research Alliance Ireland (FARA)
Monika Benson	Dystonia Europe

You can find more information about our ePAG representatives here: http://www.ern-rnd.eu/about-us/#patientadvocates

ERN-RND Work Packages

Cross-cutting activities of the ERN-RND are structured in 8 Work Packages (WPs) each led by an ERN-RND member:

WP	WP lead	Title	Leading HCPs
WP1	Holm Graessner	Coordination, management, communication and quality assurance of ERN-RND activities	Universitätsklinikum Tübingen
WP2	Holm Graessner	Evaluation of ERN-RND activities	Universitätsklinikum Tübingen
WP3	Alexandra Durr	RND diagnostic pathway	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salepétrière
WP4	Marina de Koning-Tijssen	Expert RND care coordination	University Medical Centre Groningen
WP5	Maria Judit Molnar	Training, education and capacity building	Semmelweis University Budapest
WP6	Holm Graessner	Information sharing and disease resources	Universitätsklinikum Tübingen
WP7	Antonio Federico	Guidelines, pathways and best practice	AOU Siena
WP8	Thomas Klockgether	Registries and research	Universitätsklinikum Bonn

ERN-RND Disease Groups

Disease Groups (DGs) are composed of the respective experts from all ERN-RND partners. They work on Disease Group specific topics such as care standards, specific dissemination of disease knowledge, etc.

Disease Group (DG)	DG coordinator
DG Ataxia and HSPs	Rebecca Schuele-Freyer (Germany), Caterina Mariotti (Italy), Enrico Bertini (Italy), Alfons Macaya (Spain)
DG Leukodystrophies	Odile Boespflug Tanguy (France), Ingeborg Krägeloh-Mann (Germany), Samuel Gröschel (Germany), Nicole Wolf (Netherlands)
DG Frontotemporal Dementia	Rik Vandenberghe (Belgium), Isabelle Leber (France), Markus Otto (UK)
DG Dystonia, Paroxysmal Disorders & NBIA	Giovanna Zorzi (Italy), Belén Pérez Dueñas (Spain), Tobias Bäumer (Germany)
DG Atypical Parkinsonism	Thomas Gasser (Germany), Wassilios Meissner (France)
DG Huntington’s Disease & Choreas	Anne-Catherine Bachoud-Lévi (France), Bernhard Landwehrmeier (Germany), Juan Dario Ortigoza Escobar (Spain)

The work of the DGs results in disease knowledge documents that can be found on the ERN-RND website: www.ern-rnd.eu

Clinical Patient Management System (CPMS)

The Clinical Patient Management System (CPMS) is a secure IT-Platform used by clinicians across Europe to discuss patient cases without the patients having to travel. The ERN Experts (from one or more ERNs) gather in multidisciplinary panels and use CPMS to carry out e-consultations of rare and complex cases. Patient medical documents can be safely uploaded to the CPMS after a consent form has been signed by the patient. Integrated tools in CPMS allow peer-to-peer communication, viewing of digital documents and recording expert contributions. This promotes an active collaboration, sharing knowledge and experience within and across ERNs. The health professionals are ultimately aiming at an outcome either as a diagnosis, treatment, and clinical trial or other.

Table 1: CPMS use case per Disease Group

Disease Group	Case summary
Ataxia/HSPs	Diagnostically unclear and complex cases
Leukodystrophies	Diagnostically unclear and complex cases
Atypical Parkinsonian Syndromes Genetic PD	Diagnostically unclear and complex cases
Dystonia/paroxysmal disorders/NBIA	Unsolved cases after comprehensive genetic testing
Choreas and Huntington’s disease	Patients with bona fide HD-like phenotypes but unknown aetiology
Frontotemporal Dementia	To be determined

For further questions don't hesitate to contact Sanja Hermanns.
Email: sanja.hermanns@med.uni-tuebingen.de

Collaborative Platform

The Collaborative Platform (CP) is the secure online repository for all relevant network documents (deliverables, meeting minutes, contact, etc.). It is restricted to ERN users only (need to request access from coordinator) and is not to be used for the exchange of patient data.

Training and education

Winter School

The ERN-RND Winter School is an opportunity for young neurologists/residents who are interested in rare neurological disorders to receive in-depth training from internationally-recognized rare neurological disease experts.
Students will attend overview lectures with question-and-answer sessions, as well as hands-on training. They will also be given the opportunity to present their own cases.
The Winter School is free of charge for two participants per healthcare provider. Costs for accommodation or travel will be covered by the ERN-RND. For more information, please check the ERN-RND website.

Fellowship exchanges

ERN-RND offers 5 fellowships per year to young healthcare professionals for a maximum of 3 months each. Applicants must be from an ERN-RND healthcare provider and the fellowship must take place in one of the ERN-RND's expertise centres.
Candidate's criteria:

- Resident or young specialist (< 7 years after obtaining PN registration) (PhD students do not qualify). The scheme is targeted at those who are at the early stages of their training.

For more information, please check the ERN-RND website.

Training events in collaboration with other professional societies

- ERN-RND collaborates with national and European societies active in rare neurological diseases in organizing training courses for neurologists.

- Educational webinars on rare neurological, movementand neuromuscular diseases - in collaboration with the European Reference Network for Rare Neuromuscular Diseases (EURO-NMD) and the European Academy of Neurology (EAN). The webinars cover all 6 disease groups represented in ERN-RND and alternate adult and paediatric contents.
  Various aspects from more general as clinical features, examination, disease diagnosis, therapeutic interventions and disease management to specific ones as use of scales or imaging are discussed in an interactive manner.
- More information about our webinars can be found here:
  http://www.ern-rnd.eu/education-training/webinars/

- German Academy for rare neurological disorders (DASNE): Yearly meeting to discuss interesting solved and unsolved neurological cases as well as cases for the molecular therapeutic board. The meeting also includes training workshops for young neurologists in the field of rare neurological disorders. More information about DASNE can be found here: http://www.dasne.de/index.html#home

- European Academy of Neurology (EAN): The EAN task force for rare neurological diseases organizes a yearly training course in Eastern Europe.

More information about the EAN task force for RND can be found here:
https://www.ean.org/Rare-Diseases.2682.0.html

Projects with ERN-RND involvement

Solve-RD

At the moment, there is no joint ERN infrastructure specifically targeting unsolved RD cases. To tackle this issue, a core group of four ERNs (ERN Euro-NMD, ERN-Genturis, ERN-ITHACA and ERN-RND) have jointly set-up the Solve-RD project to form the basis for a joint diagnostic research infrastructure for unsolved RD cases. Within Solve-RD, the ERNs will share phenotypic and genetic data of unsolved RD cases, based on patient consents and ethical approvals for working with Solve-RD.
For more information, please visit the Solve-RD website here: www.solve-rd.eu

The European Joint Programme on Rare Diseases (EJP RD)

The European Joint Programme on Rare Diseases (EJP RD) brings over 130 institutions from 35 countries to consolidate research, care and medical innovation on rare diseases in Europe and globally.

The EJP RD’s mission is to promote rare disease research and thus to enable effective access and use of rare disease information, research data and services to optimize exchange of knowledge between research and clinical practice. Further goals are to foster rapid scientific progress in the field of rare diseases (RD) through funding of collaborative research projects, to accelerate the translation of high potential projects as well as to improve outcomes of clinical studies. Ultimately and most importantly this project aims to decrease unnecessary hardship and prolonged suffering of RD patients.
The EJP RD brings together the resources at the national and European level involving research funders, universities, research organisations, research infrastructures, hospitals and patient organisations.
All 24 European Reference Networks are involved in the EJP RD with at least one healthcare provider per Network as official EJP RD partner. Through them, the programme links with expert centres providing highly specialized care in more than 300 hospitals across Europe, thus ultimately enabling that rare diseases patients receive the highly specialized healthcare they need. In addition, EJP RD will provide training for ERNs on cross-cutting topics and EU-wide streamlined educational program on RD research to all interested stakeholders.
For more information, please visit the EJP RD website here: http://www.ejprarediseases.org/

ERN-RND online dissemination tools

Website

Information about the ERN-RND can be found on the website: www.ern-rnd.eu which contains information on ERN-RND members and centres, CPMS and disease knowledge resources useful for clinicians and patients. It is important that this URL is shared with anyone interested or affected by a rare neurological disease in Europe so please feel free to forward it to your contacts. Please contact Alicia Brunelle for any edits to the website.

Social media

Twitter account: **@ERN_RND**
Facebook account: **@ernrndeu**
YouTube account: **ERN-RND**
Hashtag: **#ernRND**

Newsletter

We send a monthly newsletter to keep you up to date with the latest ERN-RND activities.

Acknowledgement to be used in ERN-RND publication and dissemination activities

Acknowledgement	Situation
1. " The two (or more) of the/several author(s) of this publication is/are (a) member(s) of the European Reference Network for Rare Neurological Diseases - Project ID No 739510."	A general option that members can use regardless of there being 2 or more HCPS involved. This gives attention to the existence of ERN without it acknowledging any direct input from it.
2. "This work is generated within the European Reference Network for Rare Neurological Diseases - Project ID No 739510."	An option that a partner can choose to add if the work has come into being by the work carried out by at least 2 or more ERN members working within the structure of the network.
3.“This study/project/publication/Guidelines/survey* has been supported by ERN-RND , which is partly co-funded by the European Union within the framework of the Third Health Programme “ERN-2016 - Framework Partnership Agreement 2017-2021." *choose appropriate wording	If funding is allocated to a publication/ project/etc. This will eventually apply but it is not yet the case for the moment.

Acknowledgement

ERN-RND would like to especially thank all people involved in the project for their dedication and enthusiasm to improve the care for patients with rare diseases.
This publication has been supported by ERN-RND, which is partly co-funded by the European Union within the framework of the Third Health Programme “ERN-2016 - Framework Partnership Agreement 2017-2021”.